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# NIH Clinical Center

# SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES

October 1, 1979 - September 30, 1980

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October 1, 1979 through September 30, 1980

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

# SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
# CLINICAL CENTER

## OFFICE OF THE DIRECTOR

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### General

In this past year, Clinical Center staff and Institute physicians acting under the aegis of the Medical Board have redefined responsibilities for medical care and are establishing new reporting lines and loci of accountability. They have reexamined recruitment and remuneration of normal volunteers and have proposed several changes to improve the system.

The management of the Clinical Center itself has been revised following lengthy review of functions and responsibility at the senior management level of the Clinical Center. A Department of Materiel Management has been established to facilitate movement of supplies through ACRF and Building 10. In general the Clinical Center has been moving toward a more tightly controlled management system.

The unfortunate death of a "normal volunteer" in April precipitated extensive investigation of adherence to research protocols. The records for inpatient normal volunteers were good; adherence to the formalities for outpatient research protocols needed improvement. Steps were taken by Institute physicians to ensure this.

The establishment of a Department of Critical Care Medicine was finally realized a year ago. It has contributed greatly to the quality of medical care throughout the hospital. The first Chief, Dr. Byron McLees, designed a new facility with capability for research as well as patient care. The departure of the Chief and Assistant Chief of this Department in August has forced a new mode of operation. Recruitment efforts for a new chief are underway.

The productivity of Clinical Center Departments remains high when measured by either service or research. The positron emission tomography scanner was placed in the Nuclear Medicine Department, and the Clinical Center now employs two organic chemists to prepare compounds labeled with positron-emitting isotopes. The Blood Bank has devised a simple method for obtaining neocytes to decrease the iron load of patients who require continued blood transfusions. These and other research efforts detailed in the Departmental reports are an integral part of the mission of the departments, particularly since the caliber of the staff demands both service and research.

## Mission of the Clinical Center

(1) To ensure the highest possible level of medical care to each patient;
(2) To provide optimal resources and facilities for clinical research;
(3) To perform research on methods and systems involved in patient care and study;
(4) To disseminate information to professionals and to the public relevant to clinical investigation;
(5) To develop and maintain training programs in the techniques and ethics of biomedical research and clinical research;
(6) To interact with scientists and physicians, nationally and internationally, on mutual problems of clinical research, such as policy, education, ethics, and priorities.

## Ambulatory Care Research Facility and Clinical Center Renovation

The Ambulatory Care Research Facility construction proceeded on schedule with about $30 million of the work completed during the year. The structure is complete and the mechanical and brick work is almost finished. Installation of the glass facade has begun and will be completed by close of the calendar year. The ACRF loading dock and certain below-level areas have been turned over to NIH. Center Drive, under renovation for the last few months, has been opened for use.

Two laboratory mock-ups developed by the Laboratory Committee were reviewed by the scientific staff and the agreed-upon laboratory case work has been ordered. Dedicated clinics for NEI (10th floor) and the NIMH (4th floor) were designed and integrated into the construction process. The Space Management Branch met with the Institutes to develop an ACRF accupancy and Clinical Center backfill plan.

The schedule for ACRF occupancy remains tentative. The current plan calls for NIH acceptance of the tower, top floor first, beginning in March 1981 and with complete occupancy achieved by August 1981. Significant work on breakthroughs into Building 10 has been completed without vacating laboratories. Final breakthroughs will be scheduled as close to occupancy as possible.

As the ACRF nears completion, increasing effort is being focused upon Clinical Center modernization, necessitated by facility obsolescence and ACRF interface. A nine-year program has been established to upgrade patient care units and support services, both functionally and aesthetically, and to reassign space vacated by activities relocated to ACRF. Design for the Glassware and Media Section is complete and construction has begun. The initial phase of locating surgical units close to critical care activities was completed with the design and construction of the NHLBI Surgery patient care unit on 2 West and the programming and design of NCI Surgery on 2 East along with critical care units on 2D and the 2/300 area. The program will be completed by the time the new ACRF second floor surgical suite is occupied.

## Office of the Assistant for Bioethics to the Director, CC

During the past fiscal year, this office carried forward a number of activities including:

(1) Assistance to the Director, CC, on ethical issues in protocol review with approximately 10 protocols.

Assistance to the Director, CC, on initiating a process of discussion prior to policy-making on CC rules on informed consent with children, determining death in patients who may be candidates for transplantation, and room searches.

(2) Consulted with patients, families, physicians and nurses on ethics dilemmas in treatment and research.

Total of 16 cases of requested consultation. In 6 cases, the services of Maxwell Boverman, M.D., a psychiatric consultant, were employed in order to resolve problems in human relationships that accompanied the ethics dilemma.

(3) Continued to plan and write a protocol to study the question of whether family member involvement in the informed consent process adds benefits for physician, patients, and staff.

(4) Responded to numerous requests for short consultations on questions of ethics in the planning of research, conduct of research, and the ongoing work of Clinical Review Subpanels.

(5) Supervised a bioethics intern from Greece who plans to practice law and develop a specialty in bioethics.

(6) Assisted the Department of Nursing in presenting educational meetings on informed consent and other topics in ethics.

(7) Conducted NICHD Pediatric Grand Rounds on ethical issues in perinatal medicine.

## Safety

Satisfactory progress continues towards developing a broad in-depth and effective patient care safety program. Compliments on committee activity have been received from both the Joint Commission on Accreditation of Hospitals and the Director of Safety and Occupational Health, Department of Health and Human Services.

Primary emphasis this past year related to: corridor clearance, disaster planning, "sharps" puncture program, fire safety standards, accreditation inspection, and construction plan review.

Top priority for the coming year relates to integrating the new Division of Safety program with the Clinical Center Safety Committee activity.

Office of the Associate Director

## 1. The Clinical Associate Program

Several recent studies propose that recent medical/dental graduates have shown less incentive for entering biomedical research. Recruitment of clinical associates at the NIH has been affected by this trend although it is held that the downward trend in applicants to research training programs around the country may have leveled off. The results of the 1980 Associate Matching Program at the NIH suggest that a relatively stable situation might now exist. The recruitment program this year was bolstered by an active recruiting effort that included advertisements for associates which were placed in leading medical publications. During 1980, the number of requests for applications for clinical and research associateships rose from 1,482 to 1,734. There were 290 applications received, 282 were circulated for interviews, and 162 interviewed. These were essentially unchanged from last year. Institutes participating in the NIH match successfully filled the positions available for 1981 and partially filled positions available for 1982. The caliber of applicants remains high and institutes do not anticipate difficulty in continuing to fill their positions with outstanding trainees.

The Clinical Center has revised promotional material for both the Research and Clinical Associate Programs and for the student electives. Flyers and brochures were distributed to second, third and fourth year medical students throughout the country. Promotional material was also sent to medical school's deans, student advisors and selected non-university teaching hospitals. There were 171 clinical associates, 42 research associates, and two staff associates at the Clinical Center during 1979-1980. The following chart describes the number of associates matched in 1979 through 1980 and describes the number of positions which have been filled in the 1980 match.

| | 1979 total | 1980 total | 1980 | 1981 | 1982 |
|---|---|---|---|---|---|
| CLINICAL ASSOCIATES | 62 | 59 | 7 | 41 | 11 |
| DENTAL CLIN. ASSOC. | 1 | 2 | 1 | 1 | |
| RESEARCH ASSOCIATES | 19 | 10 | 1 | 9 | |
| STAFF ASSOCIATES | 0 | 3 | 1 | 2 | |
| PHARM. RES. ASSOC. (PRAT) | 1 | 4 | | 4 | |
| TOTAL | 83 | 78 | 10 | 57 | 11 |

Applicants matched this year represented 40 US medical schools and five overseas institutions. They had recently trained at 47 hospitals in the US.

The 1980 program was reviewed by the Education Committee. During 1980 revisions in the standard associate application forms were completed and approved by the Education Committee.

## 2. Recruitment of Minority Students and Medical Graduates

During the past year the Clinical Center (Dr. Shapiro, James Alexander, Clinical Center EEO Coordinator) has engaged in the following initiatives designed to increase minority participation in the Associates Training Program:

A. Visited Duke University, North Carolina, Boston U., Howard, Tufts, Meharry, Tulane and Morehouse Medical Schools to provide minority students with information regarding NIH programs and to encourage them to apply.

B. Participated in regional meetings of the American Medical Student Association and the annual meeting of the Student National Medical Association.

C. Conferred with representatives of various medical schools at the annual Minority Biomedical Support (MBS) Symposium.

D. Conducted a conference of Minority Medical Faculty and Administrators for the purpose of designing minority recruitment strategies.

E. Participated in the annual meeting of the National Association of Minority Medical Educators.

Efforts to date have not begun to significantly change the composition of the NIH Associates. Of the 78 applicants selected in the April, 1980, matching process only four were minority (one black, two Asian and one Hispanic).

We are, however, encouraged that as more minority medical students, interns and residents become aware of NIH programs, the number of applications from this group will increase. The payback provisions of the National Health Service Corps continues to adversely impact our ability to attract many minority medical school graduates who are recipients of financial assistance under this program.

We have achieved a modicum of success in the recruitment of minority medical students for the NIH Summer Program. There was a significant increase in the number of minority applicants for this year's program. Our efforts in this area should be intensified and success will be contingent upon the support and cooperation of Institute Scientific Directors.

We have encouraged minority students to apply for the Clinical Electives Program and we anticipate that the number of minority participants which is currently insufficient, will increase as our outreach efforts begin to pay off.

## 3. The Clinical Electives Program

During 1980 electives were offered in anaesthesia (primarily a Georgetown University elective), endocrinology and metabolism, human genetics, hematology-oncology, medical and surgical oncology, immunology, nuclear medicine, pediatric psychopharmacology and adult psychiatric pharmacology. The elective in computer science was not offered this year, but it will be offered in the coming year under the direction of Dr. David Rodbard. There were 180 applicants to elective programs during 1979-1980, and 120 students from 57 medical schools were selected in the 1979-1980 Elective Program as compared to 115 students who participated in 1978-1979. Meetings were held with students during their stay at the Clinical Center in order to evaluate their educational experience. A particular effort was made to encourage participation by students at minority schools in both the Electives Program and the COSTEP Program.

## 4. Continuing Medical Education

The Office of the Associate Director in concert with the Education Committee and the staff of FAES has reviewed several courses and symposia presented both at the Clinical Center and off-site for category 1 educational credits. Courses were evaluated according to criteria for continuing medical education as published by the Liaison Committee on Continuing Medical Education. Twenty educational programs sponsored by 10 BIDs received category 1 credit during the year bringing the total number of courses approved over the two-year period to approximately 50, several of which are on-going. Programs approved for category 1 credit are marked with an asterisk when listed in the NIH Calendar. Category 1 credit as currently defined is applicable to the AMA Physicians Recognition Award and for category 1 educational credit of the Liaison Committee on Continuing Medical Education. This dual recognition is the result of a recent split in the membership of the Liaison Committee on Continuing Medical Education since the AMA has seceded from the parent organization. The Clinical Center has continued to seek recognition for its CME programs through the Liaison Committee on Continuing Medical Education. The authority for approval of CME courses was granted to the Clinical Center for a four-year period by the Liaison Committee on Continuing Medical Education in 1979.

Approval of CME programs has included a request that sponsors of such programs give consideration to evaluating the quality and effectiveness of each educational event. These evaluations have been reviewed with the sponsors and appear to be of value in planning new conferences.

## 5. Clinical Center Departments

A. The Medical Information System (MIS): A complete report on the Medical Information System can be found on page 11 . The Medical Information System has been fully implemented in the hospital for approximately two years. During the past year, this office assisted with the initial evaluation of the MIS system which included reports by Pharmacy, Diagnostic Radiology, the Outpatient Department, Nursing and clinical associates. A comprehensive questionnaire was developed by OCAMS and completed by departments, physicians and by individual nursing units. The results of this evaluation may be summarized as follows:

Clinical associates had a positive response with regard to the accessibility of MIS-generated reports in the chart, however, they were sharply divided as to the convenience of the format of the printed record. Physicians generally agreed that the benefits of the MIS system to patient care outweighed the drawbacks due to screen inflexibility or the bulky chart. A committee chaired by Dr. Griff Ross has proposed modifications to deal with both the computer generated record and lab and X-ray reports. The Nursing Department indicated that with few exceptions the functions performed by MIS were extremely useful. Pharmacy and Admissions reported that the system allowed for effective communication between those departments and patient care units. A long range formal evaluation of MIS which has been contracted to the ANSER Corporation is currently underway. An outstanding achievement accomplished by the staff in OCAMS was of the Honeywell laboratory computer interface with the MIS-IBM system. This has allowed a rapid retrieval of laboratory results which has had a very positive influence on patient care.

B. Medical Staff Affairs: The Office of Medical Staff Affairs (OMSA) has as its main function the coordination of the hospital's Quality Assurance Program (QAP). In this role OMSA was the clearinghouse for all intramural clinical research projects and provided the required staffing for Medical Board committees.

Approximately 150 new clinical projects were approved over the last year bringing the total number of active studies to over 570. The office also monitored the periodic review of all existing projects. This included the processing of over 400 annual reviews and 135 three-year reviews. The issuance of new regulations on research involving investigational drugs was the main source of investigator inquiries requiring OMSA responses.

As part of the credentials function, almost 350 physicians and dentists had their clinical privileges redelineated and their health status certified. Seventy new applications for clinical privileges were processed by the office and forwarded to the Credentials Committee. Forty-four guest medical staff and twenty-five clinical care consultant applications were approved. In addition, one nurse practitioner was granted staff affiliate status.

Early in the year the office became the focus for developing the risk management program. Risk management is a mechanism for anticipating and reducing the risk of potential people and system failures. One of its main responsibilities is to educate hospital staff to provide an environment that responds to both human concerns and physical needs of its patients, visitors, and staff members. The identification of situations in the hospital that are susceptible to potentially hazardous incident is the most important step in a risk management program. To this end a new incident reporting system was developed. Unlike previous efforts this system includes provisions for formal tracking and follow-up of reported incidents. Plans for the coming year include publicizing the system and coordinating reporting efforts with the Division of Safety and the Protection and Security Management Branch, DAS.

C. The Normal Volunteer Program: Report is included on page 37 .

D. The Surgical Administrative Committee: The air-conditioning and heating systems in the 10A surgical wing were extensively discussed by the Surgical Administrative Committee. This lead to an evaluation and readjustment of the current air-conditioning system. A more extensive evaluation by the Design Engineering Branch was proposed and this is currently underway.

The Surgical Administrative Committee reviewed the occurrence of infections in the 10A operating area and proposed to the Medical Board a series of recommendations for tightening infection control in the surgical suites. These recommendations were received and approved by the Medical Board and are currently under implementation. The Surgical Administrative Committee also toured the construction site of the ACRF operating room areas. The committee has advised Clinical Center architects on construction of both the surgical intensive care and the medical intensive care units to be located in the ACRF.

E. Cardiopulmonary Resuscitation: Representatives of the Department of Anaesthesia, Occupational Medical Services, the Clinical Center CPR Committee and Nursing met to review training available for NIH staff in cardiopulmonary resuscitation. The cardiopulmonary training function will be shared by OMS and the Anaesthesia Department to provide both basic life support training and advanced life support training. Notification of these training programs was mailed to clinical staff in the hospital with a request that physicians whose clinical responsibilities include managing patients with cardiopulmonary distress be promptly directed to the appropriate course. It is anticipated that within the coming year the Clinical Center will be able to provide a full range of life support training on site as well as retraining or re-evaluation of skills when this is required.

F. Clinical Research and Teaching: Presentations reflecting original research in osteogenesis imperfecta under protocol 79-CC-CH-14 were presented at the Fourth International Congress on Calcified Tissues, Kiryat Anavim, Israel, March, 1980, and at the Workshop on Inherited Disorders of Connective Tissue sponsored by the University of California, San Diego in June, 1980. A presentation on ocular findings in osteogenesis imperfecta was presented in collaboration with Dr. Muriel Kaiser-Kupfer, National Eye Institute, in June, 1980, at the meeting of the Association for Research in Vision and Ophthalmology (ARVO). The Associate Director also presented teaching conferences in the Department of Endocrinology at George Washington University, at Pediatric Rounds, NICHD, and at the clinical conferences of the Inter-institute Genetics Program.

## Research Accomplishments

Blood Bank investigators continued their studies on post-transfusion hepatitis, which continues to yield valuable insights into the problem. An earlier phase of the study demonstrated the existence of non-A, non-B (NANB) hepatitis, which now constitutes over 95 percent of post-transfusion hepatitis cases. Post-transfusion hepatitis caused by non-A, non-B virus is a mild disease in its acute stage, but frequently progresses to chronic liver disease. Thus, NANB may prove to be the most serious form of post transfusion hepatitis.

One of the significant outcomes of the study is that the research team has established that blood from donors with an elevated transaminase (ALT) result in significantly more hepatitis in recipients than blood from donors with a normal ALT. The Blood Bank plans to begin ALT screening of NIH blood donors and to exclude blood from donors whose values are elevated. It is hoped that this will reduce the incidence of post-transfusion hepatitis by about 45 percent. The frequency of post-transfusion hepatitis will be compared with that in their current study, with that in patients who receive Red Cross Blood (not screened for ALT), and non-transfused controls. If a practical test for NANB is developed, then such screening will be combined with ALT testing and incorporated into the same study.

The Blood Bank assumed an active role in therapeutic procedures during the past year. Numerous plasma exchanges were performed in patients with systemic lupus erythematosis, aplastic anemia, hyperlipoproteinemia, and other disorders. Many manual phlebotomies were performed on patients with polcythemia and hemochromatosis. Approximately 50 automated red cell exchanges are completed each month, giving the Blood Bank the largest reported experience with this procedure in the world. The department is now recognized nationally as a leading center for therapeutic apheresis application and research.

Members of the Clinical Pathology Department have expanded their studies on the human factor VIII/von Willebrand factor protein. They established that individuals with hemophilia A have a protein identical to normal in all respects except that it lacks clot-promoting activity, while in von Willebrand's disease it was found that the protein is quite heterogeneous. In some patients there is a quantitative defect, a complete absence of the protein and all its associated biological functions. In other patients there is a qualitative defect in which protein is present in normal amounts, but is deficient in biological activity. The research team found that the carbohydrate moity of factor VIII/von Willebrand factor protein is most important in its interaction with platelets and vessel walls and may play an important role in the maintenance of normal hemostasis and development of atherosclerosis.

Investigators from the Rehabilitation Department and Diagnostic Radiology are testing the diagnostic capabilities of ultrasound in diseases causing oral-motor dysfunction. Ultrasonic scanning of the tongue has use in the diagnosis of neurological conditions that affect talking, chewing, and swallowing and provides a measurement of progression of oral-motor dysfunction.

A real time, B-scan ultrasonic imaging system visualizes dynamic motions of the tongue during speech. A closed-circuit television system allows simultaneous monitoring of the speech and ultrasonic signals. To evaluate oral function in the past, researchers had to impose awkward procedures which interfered with normal articulation. This new system allows the subject to speak normally. It also allows comparison and retrieval of multiple repetitions of speech samples in a digital format that can be subjected to computer analysis.

Patients articulate a set of phenomes and syllables to test their ability to utter sounds. A closed-circuit television system combines the subject's voice, the front and side views of the face, the ultrasonic scan, and the processed auditory signal from the microphone to form a composite video image. The composite is recorded and stored permanently on videotape for later analysis.

## EEO

The impact of the Garcia Amendment to the Civil Service Reform Act and the transfer of the Federal Equal Employment Opportunity Program from the Office of Personnel Management to the Equal Employment Opportunity Commission mandated that agencies intensify their affirmative action efforts.

Fiscal Year 1980 was a transition year designed to introduce a systematic approach to affirmative action planning and program development. This was expected to be a results-oriented process, with emphasis on quantifiable programs. The transition year involved two interrelated phases which will lead to the development of comprehensive, affirmative action programs, developed on a multi-year basis, beginning in FY 1981.

The Clinical Center received preliminary guidance from the office of the Deputy Assistant Secretary for Health Operations regarding steps that should be taken to ensure that agencies are in compliance with Public Health Service expectations regarding affirmative action planning.

Specifically, we determined those occupational areas in which minorities and women are underrepresented; compiled position turnover data by race and sex; and began the process of establishing numerical targets designed to correct underrepresentation. These activities took place in concert with NIH-wide Affirmative Action initiatives coordinated by the Division of Equal Opportunity.

During FY 1980 the Clinical Center continued to engage in activities designed to increase minority participation in the Clinical Elective and Clinical Associate Programs. Specifically, the activities included visiting both minority and selected non-minority medical schools with significant minority enrollments; participating in meetings of medical faculty and student groups; and conferring with representatives of additional medical schools at the Annual Minority Support (MBS) Symposium.

EEO Special Achievement Awards were presented to Mr. Steven C. Groban, Chief, Outpatient Department and Ms. Linda Lawrence, Chief Technologist, Clinical Chemistry Service, Clinical Pathology Department.

## Office of Clinical and Management Systems

### I. Missions and Goals:

The mission of the Office of Clinical and Management Systems is to assist the staff of the Clinical Center by providing services of systems analysis, computer systems evaluation, and management engineering.

The goals are four-fold:

a) Coordinate the planning, development, implementation, and operation of all computer and automated systems within the Clinical Center;

b) Provide working liaison between the Clinical Center, the Division of Computer Research and Technology, and the various institutes to assure optimal and integrated clinical management and information systems;

c) Assist Clinical Center Management in application of techniques of operational planning; facility development; resource allocation; and program evaluation and review; and,

d) Initiate and conduct research and education programs in clinical and management systems.

### II. Department Activities:

A. Medical Information System: Activities surrounding the Computerized Medical Information System (MIS) continued to occupy the largest proportion of the office's activities during this year.

With the completion of the implementation of MIS for inpatient clinical care services and the direct connection of the MIS system to the Clinical Pathology Laboratory Computer System for requesting tests and reporting results, attention was shifted to the implementation of MIS in the Outpatient Department. Using the findings of the Outpatient Department reorganization plan, the MIS Outpatient Implementation Committee met regularly to plan and implement a carefully phased introduction of the MIS system into the Outpatient Department. The approach selected differed from that used for the inpatient nursing units, recognizing the unique characteristics of the Outpatient Department. A phased implementation based on installing one function at a time throughout all clinics was selected. Ordering Dental Clinic consultations was the first function selected. In addition to permitting physicians to order Dental Clinic consultations for outpatients, the clinic clerk staff was trained to assist physicians by placing the consultation orders, upon the written request of a physician.

Since the clinic clerks would thus be using MIS more intensively than previously, a special training course in medical terminology was designed specifically for the outpatient clinic clerks and taught over several weeks. Departmental tours for the clerical staff were also conducted to more fully acquaint them with the individuals and medical procedures relevant to their new assignment. This course was quite successful. Several departments suggested the value of a return visit at a later date, and consideration is being given to developing similar short courses to orient other Clinical Center staff to Clinical Center departmental activities. Subsequent to the installation of Dental Clinic consultation, Diagnostic Radiology and Nuclear Medicine consultation requests were added to MIS for outpatients as well. In conjunction with the addition of these three services to MIS, a new request for outpatient services was developed and tested. This form, although still in a trial stage, will ultimately replace as many as ten separate forms currently used to request clinical services. This multi-purpose form, together with its Clinical Pathology test request counterpart, will ultimately be used for emergency ordering, for back-up purposes should MIS be unavailable, and for requesting services in the Outpatient Department when a physician is unable to use MIS. The remaining steps in the implementation of MIS in the Outpatient Department include the addition of consultation ordering for other departments including Rehabilitation, ECG, Pulmonary Function, EEG, Nutrition, and so forth. Following this step, the Pharmacy Department will be next, with medication order entry to be done only by members of the Pharmacy staff or physicians because of the complexity, care, and legal requirements associated with medication ordering for Clinical Center patients. The final stage of patient implementation will include nursing activities and the production of various computer printed summary reports for inclusion in the Medical Record. These reports will require seven-day summaries rather than the daily summaries used for inpatients. Complete implementation is anticipated by December 1980.

B. Revisions to the MIS system: Revisions and additions were in three categories. In the first category, many programs were added to make the system faster and more reliable. Changes of this type are often not evident to those using the system; however, they are essential in permitting increased use and improved system performance to permit the addition of other features desirable to the Clinical Center. Two major application program releases and two major new system releases were installed. In the second category of changes, several programs specifically contracted for by the Clinical Center were received and installed. Among these were four programs permitting far more flexible and intelligible presentation of laboratory results at the MIS display terminals. Physicians are now able to retrieve more results than

previously, each display is easier to read, and retrieval may be made by medical groupings, such as coagulation tests, CBC's, thyroid function studies, and so forth. With the basic capabilities in place we are continuing to experiment with additional medically significant groupings. Additional programs are now in place that will ultimately allow us to simplify the ordering of laboratory studies. Using these programs, we will be able to permit ordering of laboratory studies on a "day-of-the-week" basis such as "CBC Monday, Wednesday, Friday," or "Electrolytes Q4HX3". Substantial changes were made in various nursing care documents; and nurse discharge care planning was installed throughout the hospital. In the third category of changes, numerous additional local changes including protocol order set creation and modification, enhancements to existing MIS screens, and the creation of new screens were completed. Over 4,000 changes have been made to MIS since its installation in the Clinical Center four years ago.

Because the current contract for MIS services expires September 30, 1980, extensive efforts are in progress to review the MIS specifications and contractual arrangements to assure continuity of service in the future. Preparations are under way to extend the current contract while preparing for a full evaluation, assessment of needs and recompetition for MIS in the next two years.

C. Clinical Information Utility: The Clinical Information Utility, which stores medical information at DCRT and retrieves it on request for medical researchers in the various institutes, began enlarging its role in serving the needs of the staff throughout the campus. In addition to providing individual researchers with numerous retrievals on laboratory, medication, diagnosis, and biographic data in various combinations, the CIU also became a valuable tool to the Quality Assurance Committee of the Medical Board in streamlining the process of performing medical audits, both in selection of sample records and in analysis of the content. The CIU data base has become an integral part of the medical audit process and makes possible the completion of audits in a more timely fashion with a more thorough review than is possible under purely manual methods.

D. Laboratory Computer System: The Chief, OCAMS, continues to serve as the Chief, Laboratory Computer Service, Clinical Pathology Department. The complexity of the MIS-laboratory computer link necessitates close oversight of system changes, enhancements, and development. In practice, the laboratory computer has become a specialized MIS sub-system requiring on-going coordination and control. Because of the age of the existing Honeywell Laboratory Computer System, the Laboratory

Computer Service, in conjunction with other members of the Clinical Pathology Department, initiated a study of Clinical Pathology Department computer support needs. Seminars for reviewing existing systems and possible options for the department were conducted. A set of requirements and a request for proposals is anticipated by the late fall, 1980. The specifications will incorporate both Clinical Pathology Department needs and a plan for closer system integration with MIS.

E. Workload reporting and budgeting system for Clinical Center Departments: During the year, the RMS (Resource Monitoring System) continued to serve as the Clinical Center's portion of the agency-wide manpower management program. Steps were begun to update the nursing portion of the RMS to reflect more accurately the utilization of manpower in nursing service for the coming years. OCAMS staff joined with the financial management office to develop a new set of budget reporting documents. These documents were developed to help department heads monitor their budget activities in a timely and accurate fashion. With this year's emphasis on cost containment, the executive office and departments were better able to monitor their use of funds.

F. Medical Record Improvement Projects: Staff was involved at several levels in maintenance and improvement of the quality of medical records. First, a staff member chaired the Medical Record Forms and Systems Sub-committee of the Executive Medical Record Committee of the Medical Board. This sub-committee was instrumental in screening new forms proposed for inclusion in the medical record as well as in defining a large number of forms which are no longer to be used or kept in stock. The "Medical Record Improvement Project" Committee addressed issues of chart bulk as well as usefulness of information as it is presented in the medical record. OCAMS staff provides the support to this project group in questionnaire design and evaluation, coordination with DCRT, and systems analysis to enable recommendations of the committee to be integrated with ongoing operations in information handling throughout the hospital.

In conjunction with staff members from DCRT, several prototype reports to more effectively and more compactly portray medical information have been developed. These prototype reports using actual patient data have been circulated among the medical staff for comments and suggestions for improvement. The first report, containing clinical pathology data, will be used on a continuing production basis beginning July 1980, replacing our earlier permanent clinical pathology patient chart reports. This new report will present far more data, compactly, more intelligently,

and in clinically appropriate test groupings. Similar summaries of vital sign data have been tested using patients in the NCI hyperthermia program. New summaries soon should be in use for Diagnostic Radiology, Nuclear Medicine, and Blood Bank reports as well. These new reports should contribute to the clarity of the record while substantially decreasing its bulk.

G. Outpatient Department Reorganization: OCAMS staff provided professional assistance to a study of operations of the outpatient clinics and a recommended reorganization plan. This study incorporates plans for the introduction of this function into the clinic, the transition of the present Outpatient Department to the ACRF, and changes in the philosophy of providing the services required for outpatient care. Coordination of these changes with MIS was essential because of overlapping functions including the need for MIS patient appointment scheduling function and changing duties and responsibilities for the clinic staff.

H. CLINFO Test Site: The OCAMS staff continued to interact with the medical, administrative, and data processing staffs of many U.S. and foreign hospitals and university medical centers who are in the process of assessing their needs for MIS-type systems in their institutions. The experience with MIS at the Clinical Center has provided a rich source of unique information for these colleagues in the field. Presentations included a discussion of interfacing multi-vendor systems at the American Hospital Association and an invited presentation to publish Public Health Service clinical laboratory directors on laboratory computer systems. One staff member serves on the USPHS Career Development Committee. The staff is also represented on the Executive Committee of the Maryland Hospital Education Institute. He participated in the development of patient safety standards for the American College of Surgeons and the development of state-wide nurse recruitment and retention standards. The staff participated as faculty for the Medical Record School of the USPHS in Baltimore by developing and presenting a series of lectures in "Computers in Medicine." One staff member also served as Program Chairman for the Annual Meeting of the Health Services Division of the American Institute of Industrial Engineering.

K. Staffing: OCAMS staff was augmented by the addition of an experienced industrial engineer to assist in long-needed management analysis studies. Initial activity will be in the Materiel Handling Department and assistance to the Nutrition Department in conversion to a central tray system. Recruitment is under way for a physician with medical computer system experience and interests to support long-range Clinical Center computer system planning and installation activities.

L. MIS Evaluation: A contract was awarded using HHS set-aside funding for a fifteen-month extensive evaluation of medical computer system use at the Clinical Center with particular emphasis on the Medical Information System. The evaluation will focus on the use, effectiveness, operations, benefits, costs, technology, and evolutionary potential of the computer systems within the Clinical Center. Techniques will include questionnaires, personal interviews, time and motion study, and assessment of the hardware and software technology used to implement and support MIS. The result of this study, together with independent Clinical Center efforts, will establish the guidelines for computer system support of clinical care and research throughout the 1980's at the Clinical Center.

M. Computer System Privacy and Security: Because of the increasing HHS requirements for computer system privacy and security, one staff member now devotes substantial time to understanding, assessing, and reporting the compliance of all Clinical Center Medical Computer Systems with HHS and OMB standards. This individual participates in the NIH-wide ADP security program. A program of technical requirements and associated budget will be developed for the Clinical Center in conjunction with these activities. In addition, a small Clinical Center task force has been established to determine what data each individual using MIS may retrieve and use. For example, should a laboratory technologist be permitted to view medications that a patient has received? Tentative recommendations for appropriate access are being reviewed by Clinical Center department heads at the present time. Upon completion, this matrix of user category versus information access will complete one of the requirements of the ADP security guidelines.

## III. Future Objectives:

A. Completion of the MIS installation for the outpatient services is a primary objective for the coming year. Completion on a phased basis is anticipated by December. With completion of the Outpatient Department, MIS can be evaluated as a "total" hospital information system. In addition, accurate and timely statistics of departmental workloads and activities will then be available through MIS for hospital planning, for budget office use, and for manpower reporting under the Resource Monitoring System.

B. With more and more capabilities added to MIS, less and less reserve capacity is available on our central computer system. In addition, sharing the Saint Barnabas Hospital computer system for emergency back-up is no longer feasible during prime hospital working hours. Negotiations are under way to obtain additional computer equipment dedicated to the Clinical Center Medical Information System.

C. The Clinical Pathology Laboratory Computer System has been in operation for five years, its expected lifetime when the contract was awarded in 1974. The equipment itself is no longer in production and steps must be taken soon to insure a smooth transition to a more modern system which will continue to meet the needs of the hospital. Clinical Pathology Department requirements are being collated, options are being reviewed, and issuing of an RFP is anticipated for early FY 1981.

D. Staff support will be sustained for the Medical Record Improvement Project. These will be directed toward the final design and logistics involved in a greatly improved presentation of Clinical Pathology data for the physician in patient care and research. The other thrust in this project for which OCAMS will have major responsibility will be in attempting to change the form in which major sections of the medical record are kept from paper to electronic storage medium.

E. With the reorganization of the Financial Management Office, CC, and the further revision of budget reporting and control systems, OCAMS has as an objective the complete integration of the Resource Monitoring System for workload and manpower management reporting into the budget process and the transfer of operational responsibility for this to the FMO.

F. Additional OCAMS support will be required for several Clinical Center departments seeking to improve services and add capabilities through the use of automated techniques and better work management. A combination of management engineering studies and computer systems support may be anticipated for the Pharmacy Department, Nutrition Department, and the Medical Record Department in particular as they seek to use advanced computer systems for departmental functions and management activities. The proper integration of these departmental requirements and systems with existing Clinical Center computer-based information systems is essential to avoid escalating costs and personnel commitments while maximizing service provided.

G. The development of a long-range plan for medical and hospital information management will be a major focus of OCAMS. Increasingly, organizations must regard information as a critical component in planning, decision-making, and organizational function. The cost of acquiring and utilizing information in all large organizations is a substantial part of the organization's budget. The cost of not managing information effectively may be even higher. Information as a Clinical Center resource will be studied and recommendations concerning the use of this resource will be formulated during the coming year.

## Office of Clinical Reports and Inquiries

Clinical Center information, publications, press, and public affairs activities are centered in the Office of Clinical Reports and Inquiries. The office is responsible for advising the Director and Executive Staff on ways to enhance the Clinical Center's public and professional image as a preeminent clinical research facility, and on the effective interpretation and reporting of research findings produced within the Center. These findings are of interest and concern to many audiences, including Congress, the Department and other Government agencies, scientists, physicians, voluntary health agencies and the general public.

The Office initiates many programs and responds to Congressional and Departmental, NIH, and internal and public requests. It keeps all Clinical Center personnel informed of hospital activities, provides all hospital departments with communications assistance, and supports the functions of the CC's hospital service departments to ensure the delivery of the highest quality of patient care.

## Staff Communications

Physician Recruitment: The OCR&I continues to support the Associate Director's Office in an aggressive national recruiting campaign to attract top candidates to the NIH medical elective and associate training programs.

The recruitment plan calls for direct mailings of recruitment materials to medical students and residents throughout the year. The mailings are scheduled so that students and residents informed of the programs at a period in their education when coming to NIH to study or serve as an NIH associate would be a logical step in their medical or research training.

This year the OCR&I updated and expanded mailings of recruitment materials and will again arrange for their distribution. More than 28,000 Clinical Electives flyers and catalogs and 77,000 Associate Program flyers and brochures were mailed last year.

Selective mailings of posters and catalogs to key individuals and institutions that disseminate or make the information available to medical students were also coordinated. Complementing this effort is the continued use of journal advertisements to recruit physicians for specific medical fields or to offer information on fellowship programs available in the Institutes.

This office also coordinated the display of the Associate Training Program exhibit at professional meetings. An OCR&I staff member accompanied the NIH Associate Training Program exhibit to the Student National Association in Hartford, Connecticut in April 2-3.

The results of the recruitment effort are encouraging. Student and resident response to this campaign has shown a steady increase in application requests in the three years during which the plan has been in effect. It is especially important that the intensity of the recruitment campaign

be stepped up when the ACRF opens and the demand for physicians to staff the facility increases.

Department Pamphlets and Displays: The OCR&I has placed a high priority on supporting the CC departments in their publication needs. The office has promoted employee communications as an effective method to train and inform them. It is also hoped that presenting employees with clear, well-written and informative publications will build and strengthen a sense of unity within the hospital.

Last year the information office redesigned most of the CC publications in a new format. All new publications now conform to the new design, which results in a unified image for the CC. A logo was developed, which will identify CC publications and it is now being used on all materials originating from the Clinical Center.

Publications were prepared or revised for a number of departments including the Nursing Department, NIH Volunteer Office, Office of Clinical and Management Systems, Clinical Pathology, Blood Bank, Medical Records, Rehabilitation Department, Nutrition Department, Outpatient Department, Admissions Department, and Pharmacy.

Closeup: The employee newsletter provides employees with news about events taking place around the CC and the people that work here. The monthly newsletter featured stories on the opening of the Blood Bank Pheresis Unit, the new Surgical Services Department, Hispanic-American Week and Black History Month, and a visit by HHS Secretary Patricia Harris. Closeup also reported to employees on the visit of the top health administrators of the People's Republic of China and a visit of the USSR delegation of scientists to the Blood Bank.

The editorial board continued to function as a forum for discussion of new stories and suggestions for improving Closeup. The newsletter benefited this year by the assistance of two information interns, two summer employees who were journalism students, and a normal volunteer on a career assignment. All of them contributed ideas for stories and several articles for Closeup. The editor of the paper attended a course on In-House Publications.

Director's Update:

The information office continued to coordinate the preparation, printing, and distribution of the Director's newsletter. Director's Update communicates clinical and administrative information to staff physicians. Using the newsletter as a forum, the director discussed several issues, such as medical audits, medical records and the privacy act, and a new ruling that X-rays and laboratory tests are no longer mandatory when a patient is admitted to the CC.

Many of the Clinical Center departments contributed articles on topics such as transfusion problems, crisis limits for key laboratory analyses, and correct procedure for collecting blood gases samples.

## Patient Communication Program

The information office is developing a comprehensive communication program for Clinical Center patients. These efforts include publications, closed-circuit television, and videotapes produced by this office.

A series of leaflets on more than 50 tests and diagnostic procedures are now available to patients. They were developed by the Nursing Department and edited by this office.

A booklet on informed consent entitled "A Patient's Guide to Research at the Clinical Center" was developed by this office from a manuscript written by Drs. John Fletcher and Philippe Cardon. It has been well received and is being used extensively in the Clinical Center.

Another facet of the effort to inform patients of their rights and responsibilities is the development of a videotape called "The Right to Know." A script was written based on material provided by Drs. Fletcher and Cardon, which reinforced the main points of informed consent presented in the booklet, and provided a brief explanation of research procedures. The videotape was completed early in the year with the help of the NIH Audio-visual Section and a contractor editor. The tape is being shown twice a day on the closed circuit television channel dedicated to patient education. The nursing department has been given a copy to show to patients and their families on an individual basis. "The Right to Know" was also viewed by groups of new associates as part of their orientation to the Clinical Center.

## Patient Education Television Channel (CCTV):

The Clinical Center Television system (CCTV) on channel 10 is devoted to health-related programs, which offer patients an opportunity to learn about issues that affect their health. They are offered programs on particular diseases, such as arthritis, emphysema, heart disease, and information on medical procedures. Medicine for the Layman lectures and scientific programs, such as the award-winning Smithsonian and NOVA series are shown. Programs on life styles, recreation, and relaxation provide a change of pace.

The CCTV was started in late February. Some technical problems developed, but they were resolved and a month later the system was running smoothly. The Television Advisory Board met several times during the year to offer suggestions, advice, and guidance on the patient education project. The Nursing Department and several physician-experts were extremely helpful in reviewing the programs for accuracy, content, quality, and suitability for the patient TV system. The Television Engineering Section has handled the technical aspects of the system.

Programs, publicity flyers, tray cards, and TV stickers were developed with the assistance of the Graphics Design Section, MAPB. The Patient Activity Section distributes the programs each week with their patient news letter. The tray cards are distributed once or twice a month through the cooperation

of the Nutrition Department. A CCTV sticker has been placed on all television sets to remind patients to tune in to channel 10.

Plans for the future include expanding the programming to eight hours daily, intensifying the CCTV publicity, drawing up a plan for outpatient viewing of selected programs, and improving the general technical and program quality. Feedback from the patients is necessary at this point and it is planned to survey them when the new patient education coordinator comes on board. We need to find out how many are viewing CCTV, what they might prefer in programs, and which programs now shown are the most successful. This information would be helpful in planning future programs and in planning where the system is to go in the next year. The Clinical Center has the capability to put live events on the system and this year we will show some of the Medicine for the Layman lectures in the evening.

It is recognized that the attraction of commercial television is formidable. In order to draw patients away from that medium requires excellent programming, well-planned continuous publicity, and support from the Nursing Department to encourage patients to watch CCTV.

## Patient Communication Coordinator:

This year a patient communication coordinator was recruited with the view that this person would plan, coordinate and unify the program at the Clinical Center. The role of the coordinator would be to initiate, facilitate, and assist in the development of patient education programs at the hospital. The patient communication coordinator would work closely with the departments to work out their education programs. Several departments have already embarked on programs and it is important to integrate them into an overall plan.

The coordinator will survey the departments to find out what educational programs are needed and what programs are already in progress. Using the survey as a base for assessing the needs of the departments, the coordinator will develop a comprehensive plan, establish priorities, and assist with the implementation of the programs. An important aspect of the process will be evaluation of the programs and testing their effectiveness.

## Television Engineering Section:

Last year the Television Engineering Section became part of an operating component of the OCR&I. The Chief of the Section, Mr. Will Whitehouse, retired on June 1. Ms. Sandra York was appointed Acting Chief and has been serving in that capacity since Mr. Whitehouse's departure. She has been in charge of supervising the day-to-day operations, as well as the technical operation of the closed-circuit television system. Television engineering personnel edits the various videotape programs into segments of one-hour duration in order to facilitate continuous showing of the videotapes. A completely automated system which would free personnel from tending the system so closely is being considered for purchase next year. When television closed circuit programming is expanded to a full eight hours, the automatic system will be a necessary acquisition.

A major segment of this Section's work is to give audiovisual support to Institute research programs in the Clinical Center. Diagnostic procedures are videotaped and played back on request or transferred to disk for frame-to-frame analysis. As a result of the Section being a central viewing facility, all images relating to a single patient (e.g. the cineangiograms, echocardiograms, and the Nuclear Medicine ventriculograms) can be shown to an investigator. The Section is now working with the following branches:

Cardiology Branch, NHLBI

Support consists of videotaping ventricular cineangiograms, coronary arteriograms and the newly instituted procedure for coronary dilitation. Extensive use is made of the television facilities to record, playback, and analyze the video image for data pertinent to the patient's diagnosis and care (e.g., ejection fraction, and regurgitant index).

Echocardiography Branch, NHLBI

Videotape recordings are made of echocardiograms for immediate diagnostic review, for playback at conferences, or for transference to video disc for frame-by-frame analysis (e.g., measurement of left ventricular dimension, or wall thickness).

Diagnostic Radiology

The staff is on call for videotaping and playback for numerous procedures carried out in the Diagnostic Radiology Department (e.g., barium swallows, voiding cystourethrograms, and arteriograms).

These are either played back for immediate review, held for playback at conference time or used in the stop-motion mode for direct photography as a permanent record in the patient's chart.

Ultrasound

A real time ultrasound scanner, the Learle B scan format, the NBS Computer enhanced image or the ADS linear array scan are sent to TV Engineering for recording playback and still-frame photo-documentation. Videotape recordings of ultrasound gall bladder studies are being recorded at this time for future frame-by-frame analysis.

The image from the ultrasound real-time scanner has been used in conjunction with television or fluoroscopy image, audio signal, and averaged audio wave form in a study of dynamic motions of the tongue during continuous speech. At this time these video recordings are used both as diagnostic tools and as a teaching aid.

Neuropthalmic Section, NEI

Neuropthalmic section employs Television Engineering to analyze eye movement recordings, and to edit video recordings which are then presented at conferen

## Diagnostic Methodology

This section is actively engaged in the computer analysis of video images derived from dental radiographs. Contrast enhancement, differentiation of edges and crispening techniques are applied to the computer images. Our function will be storage of dynamic transforms for later replay and development of the intercommunication capabilities between various branches who are engaged in computer analysis of video images.

## Nuclear Medicine

The computerized television monitor reported last fiscal year as being purchased by Nuclear Medicine does not interface with our equipment. Their recordings can be dubbed, but cannot be played back or video processed.

The purchase was made without consulting with the Television Engineering Section. Efforts will be make to assist and advise CC departments when purchasing equipment which must be compatible with the CC television system.

## Laboratory of Parasitic Diseases

An extensive television system using low-light level cameras is employed by the laboratory to visualize and record faint microscopic images under monochromatic light.

This is utilized to study cell proliferation, growth patterns and the effect of various pharmacologic agents on the cultures *in vivo*.

## Nursing Department, CC

Television Engineering Section loans the Nursing Department a mobile television recording cart with video monitor, 1/2" reel-to-reel video tape recorder, audio mixer, and video camera; and a cassette playback cart.

## George Washington University, Anatomy Department

George Washington University used the video planimeter in their research of folliculogenesis of rhesus monkeys.

## Anesthesia, CC

A television camera, video monitor, and audio mixer was lent to the Anesthesia Department, to monitor its respirator.

## Developmental Endocrinology, NICHD

Plans are being made for Developmental Endocrinology to use TV Engineering's special video equipment to count the average number of cells in the pituitary gland.

## Clinical Reports and Scientific Publications:

This office coordinated twelve Combined Clinical Staff Conferences and edited the proceedings of six of them for publication in the Annals of Internal Medicine. Approximately 28,000 notices were mailed to referring area physicians on the availability of these papers in reprint form and over 8,000 reprints went to requestors.

These conferences and the proceedings are an important means of sharing with scientists and physicians all over the world the most recent research findings, and techniques developed by NIH investigators.

The office edited 95 professional papers prepared by CC staff for publication in medical and scientific journals and provided editorial services during manuscript preparation.

Four nursing conferences were presented this year by members of the Clinical Center Nursing Department. This office helped prepare the programs and publicity, such as table tents, flyers, invitations, and posters, for the conferences. In addition, OCR&I edited the conferences for publication as monographs for distribution to nurses across the country.

This office also submitted two articles for publication in the NIH feature column in the Journal of the American Medical Association. One article described work done by the Blood Bank on neocyte transfusion for thalassemia patients to lessen the problems caused by a tendency of multiply transfused patients to overabsorb iron. The other featured a new ultrasound diagnostic technique used in diseases causing oral-motor dysfunction. The Rehabilitation and Diagnostic Radiology Departments developed the technique, which visualizes dynamic movements of the tongue during speech, to measure the progression of disease.

## Public Communications Program

One of the important functions of the Clinical Center is to disseminate information to professionals and to the public relating to clinical investigation.

## Medicine for the Layman

The OCR&I staff again coordinated the Medicine for the Layman lectures and publicity. The series was conceived by the Director of the Clinical Center four years ago. The talks are given by physician-scientists working in various fields and are presented at a level the average, well-informed adult can understand. The general approach is to describe how the healthy body or organ system functions, what can go wrong, what can be done to treat the disorder.

It was recognized that the talks provided a rich store of medical information which could be used to great advantage to inform the public of new developments in the health field. Therefore, publications based on the talks were planned and the lectures were captured on videotape.

Seven publications were printed this year and eight were edited. Several of the Institutes have shown great interest in the publications and have reprinted a number of them and are distributing them independently. For example, NHLBI has reprinted over 350,000 of Heart Attacks, and NCI printed 40,000 of Cancer Treatment.

More than a dozen videotapes have been edited and are being offered for sale through the National Audiovisual Center and on a free-loan basis through Association Films, Inc. Association Films is marketing the tapes and conducting a promotion campaign on the Medicine for the Layman series. The programs are also offered to cable television and several of them have been shown on a number of west coast TV stations. This has prompted numerous inquiries from the public about the availability of videocassettes for purchase.

## Public Inquiries

The information office receives numerous calls and letters asking about admission procedures and requesting information relating to diseases or health care. Approximately 400 patient referrals to the Clinical Center from private physicians were processed through this office.

The office also answered approximately 43 Congressional and 340 general inquiries by letter or telephone.

## Press

The Medicine for the Layman series generated considerable press and media activity this year. During the month of September, 1980, Channel 5's Panorama featured Dr. Donald Tower of NINCDS and Dr. James Balow of NIAMDD, both lecturers for the 1980 series. Four more lecturers are scheduled on a regular Wednesday afternoon slot that Panorama has assigned to our speakers. The radio spot has been aired on several stations, and OCR&I has received 35 inquiries about the series from the public. The TV spot was distributed to all the local television stations on August 6 and should generate considerable public response once the stations begin broadcasting it.

The OCR&I staff organized the opening of the CC Blood Bank's Pheresis Unit. They coordinated a press meeting to announce the new continuous-flow cell separator that will be useful in therapy of patients with thalassemia and sickle cell anemia. Using the cell separator, physicians are able to separate neocytes from a unit of blood. Patients with thalassemia require frequent transfusions, which may cause iron overload in vital organs that can endanger their lives. This new process will reduce the number of transfusions a patient requires by 50% because neocytes have a much longer life span than ordinary red cells.

In March the OCR&I provided assistance to a Public Television System (PBS) crew from Seattle, Washington, which is filming a health series called "Hard Choices." The crew is producing a program about medical ethics and the many facets of medical research. Physicians from several Institutes were interviewed for the program, which explored issues in research involving humans. The program will be aired in January 1981.

In September 1980, Canadian educational television filmed several laboratory sequences at NIH for a series entitled "Fast Forward." This series focuses on the effects of computers and high-speed communications on society. The TV crew interviewed several NIH physicians on high technology and its clinical applicability in medicine for a specific show in the series called "Medical Technology."

Time-Life books contacted the OCR&I for information to be used in their new health series. They interviewed and photographed several physicians for material to be used in the books entitled "The Physician" and "Fighting Cancer."

A photographer was sent to NIH by American Pharmacy magazine to take photographs to illustrate a feature article on cancer treatment, radiation, surgery, and chemotherapy. An OCR&I staff member accompanied and assisted the photographer on the project.

Approximately 10 press calls were received that related to the death of normal volunteer Bernadette Gillcrist. Many more calls were fielded by t CC Director's office, and NIH Information Office.

The death of Teddy DeVita, a CC patient for many years, prompted a number of press calls. These inquiries were handled by this office.

## Special Events

The Special Events staff planned, coordinated and directed specific programs for 44,081 visitors to the NIH in FY 1980. Included were 232 visitors from 49 foreign countries and 969 domestic visitors. The Section consulted, planned and provided staff assistance for 216 scientific and administrative meetings attended by 42,880 visitors in the Jack Masur Auditorium.

During the FY 1980, the Special Events Section engaged in the following:

Scheduled 236 appointments with NIH researchers

Arranged 90 film showings for 605 visitors

Conducted 161 tours for 1,054 visitors

Collected, assembled and distributed 7,963 publications to visitors

Collected, assembled and distributed 39,710 publications for lecture series "Medicine for the Layman"

Answered 1,730 public inquiries by letter and telephone

Maintained the NIH Speakers Bureau and filled 12 requests

Administered a roster of individuals and called upon them to assist in interpreting for 9 foreign visitors and foreign born patients

Maintained a current and comprehensive invitation list for all NIH lectures, dedications and ceremonies

As executive secretary for NIH Lecture Committee, was responsible for administrative arrangements for 3 NIH Lectures and 2 G. Burroughs Mider Lectures.

# NIH LECTURE SERIES

## Fiscal 1980

The Special Events Section is responsible for administrative arrangements for the NIH Lectures.

| | |
|---|---|
| NIH Lecture: | September 12, 1979<br>Solomon H. Snyder, M.D.<br>The Johns Hopkins University<br>School of Medicine<br>Baltimore, Maryland<br>Title: "Drugs, Neurotransmitters and the Brain" |
| G. Burroughs Mider Lecture: | October 17, 1979<br>Martha Vaughan, M.D.<br>Chief, Laboratory of Cellular Metabolism<br>National Heart, Lung and Blood Institute<br>National Institutes of Health<br>Bethesda, Maryland<br>Title: "Regulation of Cyclic Nucleotide Metabolism" |
| NIH Lecture: | November 28, 1979<br>Walter Gilbert, Ph.D.<br>American Cancer Society<br>Professor of Molecular Biology<br>Harvard University<br>Cambridge, Massachusetts<br>Title: "The Structure and Evolution of Genes" |
| G. Burroughs Mider Lecture: | February 27, 1980<br>Thomas Waldmann, M.D.<br>Chief, Metabolism Branch<br>National Cancer Institute<br>National Institutes of Health<br>Bethesda, Maryland<br>Title: "The Control of the Immune Response: Regulatory Cellular Interactions and the Control of Lymphocyte Differentiation" |
| NIH Lecture: | May 7, 1980<br>Baruch S. Blumberg, M.D., Ph.D.<br>Associate Director for Clinical Research<br>Institute for Cancer Research<br>Philadelphia, Pennsylvania<br>Title: "Hepatitis B Virus and the Pathogenesis and Prevention of Cancer of the Liver" |

# VISITORS DURING FISCAL YEAR 1980

## By Discipline

### A. Domestic - 969

| | | | |
|---|---|---|---|
| Medical | 41 | High School | 60 |
| Paramedical | 177 | Laymen | 18 |
| Administrative | 54 | Medical Educators | 1 |
| Hosp. Admin. | 1 | Employees | 140 |
| Teachers | 4 | Technology | 10 |
| Grad. School | 171 | State Dept. | 7 |
| College | 281 | Interpreter | 4 |

### B. Foreign - 232

| | | | |
|---|---|---|---|
| Lab. Science | 10 | Med. Educators | 4 |
| Medical | 69 | Employees | 1 |
| Paramedical | 37 | Science Writers | 4 |
| Administrative | 41 | Security | 2 |
| Hosp. Admin. | 4 | Scientific Attache | 1 |
| Teachers | 1 | Min. of Health | 21 |
| Grad. School | 18 | Interpreter | 2 |
| Laymen | 12 | Statesmen | 4 |
| College | 1 | | |

Foreign Visitors by Country of Origin - Fiscal Year 1980

| | |
|---|---|
| Afganistan | 1 |
| Argentina | 2 |
| Australia | 1 |
| Bangladesh | 4 |
| Belgium | 4 |
| Canada | 2 |
| China | 30 |
| Columbia | 1 |
| Ecuador | 2 |
| Egypt | 6 |
| England | 3 |
| France | 3 |
| Germany | 14 |
| Greece | 2 |
| Honduras | 1 |
| India | 7 |
| Ireland | 2 |
| Israel | 39 |
| Italy | 3 |
| Japan | 15 |
| Kenya | 1 |
| Korea | 1 |
| Luxembourg | 1 |
| Malaysia | 3 |
| Mexico | 2 |
| Nepal | 2 |
| Netherlands | 2 |
| New Zealand | 1 |
| Nigeria | 4 |
| Pakistan | 4 |
| Panama | 1 |
| Peru | 1 |
| Peurto Rico | 1 |
| Philippines | 6 |
| Poland | 5 |
| Scotland | 4 |
| Senegal | 1 |
| Seychelles | 1 |
| Spain | 1 |
| Sri Lanka | 4 |
| Sudan | 3 |
| Surinam | 1 |
| Sweden | 5 |
| Switzerland | 4 |

| | |
|---|---|
| Turkey | 1 |
| USSR | 12 |
| Venezuela | 1 |
| Yugoslavia | 4 |

## SPECIAL EVENTS SECTION

| MONTH | VISITORS | | | MEETINGS | | TOURS | | NIH FILM SHOWINGS | | APPT. WITH STAFF | REQUESTS FOR SPEAKERS | REQUESTS FOR INTERPT. | PUBS. DISTRIB-UTED | PUBLIC INQUIRIES |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | For. | Dom. | Total | No. | Attend-ance | No. | Attend-ance | No. | Attend-ance | | | | | |
| OCT. | 30 | 53 | 83 | 27 | 6,930 | 15 | 78 | 8 | 11 | 21 | 1 | 1 | 680 | 115 |
| NOV. | 35 | 80 | 115 | 23 | 4,825 | 12 | 115 | 8 | 70 | 13 | 1 | - | 1,094 | 140 |
| DEC. | 10 | 17 | 27 | 17 | 2,610 | 4 | 17 | 3 | 6 | 10 | - | - | 253 | 105 |
| JAN. | 10 | 47 | 57 | 11 | 1,940 | 7 | 58 | 3 | 5 | 3 | - | - | 164 | 135 |
| FEB. | 10 | 77 | 87 | 18 | 2,620 | 11 | 67 | 8 | 63 | 28 | - | - | 185 | 115 |
| MARCH | 2 | 132 | 134 | 20 | 3,655 | 11 | 103 | 7 | 81 | 12 | 3 | - | 557 | 130 |
| APRIL | 5 | 172 | 177 | 24 | 4,830 | 16 | 172 | 12 | 156 | 23 | - | - | 1,794 | 210 |
| MAY | 14 | 64 | 78 | 20 | 3,555 | 11 | 65 | 8 | 35 | 19 | - | - | 727 | 195 |
| JUNE | 23 | 37 | 60 | 14 | 1,873 | 19 | 54 | 9 | 31 | 25 | 1 | - | 359 | 190 |
| JULY | 66 | 160 | 226 | 11 | 2,320 | 20 | 195 | 8 | 120 | 48 | 2 | - | 878 | 145 |
| AUG. | 18 | 63 | 81 | 5 | 542 | 25 | 76 | 13 | 22 | 26 | 1 | - | 412 | 130 |
| SEPT. | 9 | 67 | 76 | 26 | 7,180 | 10 | 54 | 3 | 5 | 8 | 3 | - | 860 | 120 |
| | | | | | | | | | | | | | | |
| TOTAL | 1,201 | 232 | 969 | 216 | 42,880 | 161 | 1,054 | 90 | 605 | 236 | 12 | 1 | 7,963 | 1,730 |

# SPECIAL EVENTS SECTION ACTIVITIES

## Comparison-Fiscal Years 1972-1980

| | VISITORS | | | MEETINGS | | TOURS | | MOVIE SHOWINGS | | APPOINT-MENTS WITH STAFF | REQ. FOR SPEAKERS | PUBS. DISTRIB-UTED | INQUIRIES | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| YEAR | For. | Dom. | Total | No. | Attend-ance | No. | Attend-ance | No. | Attend-ance | | | | PUB. | CONG |
| 1972 | 900 | 2,846 | 3,746 | 231 | 40,785 | 211 | 1,172 | 330 | 2,760 | 610 | 23 | 32,521 | 1,185 | 4 |
| 1973 | 1,010 | 2,489 | 3,499 | 241 | 48,648 | 179 | 852 | 343 | 2,315 | 651 | 56 | 31,237 | 1,660 | 6 |
| 1974 | 529 | 2,232 | 2,761 | 194 | 47,804 | 175 | 932 | 228 | 1,340 | 804 | 37 | 21,983 | 1,620 | 1 |
| 1975 | 416 | 23,184 | 23,600 | 258 | 51,363 | 167 | 1,078 | 229 | 1,654 | 498 | 31 | 75,777 | 1,482 | 1 |
| 1976 | 510 | 22,837 | 23,347 | 68 | 19,974 | 157 | 602 | 189 | 1,799 | 504 | 9 | 69,750 | 1,433 | 0 |
| 1977 | 2,505 | 1,574 | 2,079 | 298 | 55,742 | 238 | 1,192 | 275 | 1,282 | 461 | 47 | 11,374 | 1,346 | 25 |
| 1978 | 297 | 2,374 | 2,671 | 264 | 62,360 | 240 | 1,531 | 246 | 1,352 | 363 | 28 | 9,738 | 1,501 | 9 |
| 1979 | 261 | 1,078 | 1,339 | 220 | 42,521 | 138 | 858 | 116 | 778 | 182 | 20 | 5,862 | 1,556 | 6 |
| 1980 | 232 | 969 | 1,201 | 216 | 42,880 | 161 | 1,054 | 90 | 605 | 236 | 12 | 7,963 | 1,730 | 2 |

## DISTRIBUTION OF VISITORS BY CONTINENTS

### Fiscal Years 1975 - 1980

| CONTINENT | FY - 1975 | FY - 1976 | FY - 1977 | FY - 1978 | FY - 1979 | FY - 1980 |
|---|---|---|---|---|---|---|
| AFRICA | 7 | 80 | 34 | 11 | 3 | 15 |
| ASIA | 143 | 121 | 219 | 146 | 149 | 142 |
| AUSTRALIA | 4 | 2 | 7 | 5 | 0 | 1 |
| EUROPE | 129 | 166 | 212 | 113 | 98 | 59 |
| NORTH AMERICA | 1,764 | 42,941 | 1,587 | 2,380 | 1,084 | 975 |
| SOUTH AMERICA | 25 | 11 | 20 | 16 | 5 | 9 |
| TOTALS | 2,072 | 43,321 | 2,079 | 2,671 | 1,339 | 1,201 |

## Professional Activities

Dr. Lipsett served as President of the Endocrine Society this past year. He delivered the Presidential address at the 62nd Annual Meeting of the Endocrine Society on 'The Social Significance of Endocrinology." He continues to serve as Secretary General, International Society of Endocrinology. He was appointed to membership on the Scientific Advisory Board, Technion-Israel Institute of Technology, Haifa, Israel.

Dr. Lipsett was accorded the honor of being the first recipient of the Peter Kiewit Distinguished Lectureship in Medicine and delivered an address on "Clinical Research in the Private Hospital" at the annual meeting of the Eisenhower Medical Center Board of Trustees at Palm Desert, California.

Lectures given by Dr. Lipsett included: "Estrogens and Cancer" at the Philadelphia Cancer Club; 'Hirsutism and Virilization" at Mercy Hospital Annual Endocrine/Metabolic Symposium, Toledo, Ohio; "Diagnostic Evaluation of Androgen Excess in Women" at the George Washington Postgraduate Course in Reproductive Endocrinology and Infertility; an address on "Drugs, Hormones and Cancer" at the Worcester Foundation for Experimental Biology Symposium; and "Physiology and Pathology of the Ledig Cell" at the Beth Israel Hospital Seminar in Medicine.

Dr. Lipsett participated in the Postgraduate Programme of the New South Wales State Cancer Council, where he lectured on "Key Issues in Oncology". He also attended the Sixth International Congress on Endocrinology held in Australia.

Dr. Lipsett gave an address at the American College of Physicians Conference on the Federal Regulatory Process. He served as Rapporteur for the Consensus Meeting on Steroid Receptors in Breast Cancer and presented the data at the fall meeting of the National Surgical Adjuvant Project for Breast and Bowel Cancers in Chicago.

Dr. Lipsett is a member of the faculty of the Uniformed Services University of the Health Sciences and conducted courses on ethical, legal, and social aspects of medical care. He taught an Endocrine Review Course for the Foundation of the Advanced Education in the Sciences and an Endocrinology course for the American College of Physicians.

Dr. Griff Ross was awarded an Honorary Degree of Doctor of Science, The George Washington University, Washington, D.C. He was also elected to the Alumni Hall of Fame, Stephen F. Austin State University, Nacogdoches, Texas.

Dr. Ross was an invited lecturer to the Postgraduate Course of the American College of Obstetricians and Gynecologists, where he spoke on 'The Intraovarian Hormonal Milieu and Regulation of Follicle Growth in Humans," New York, New York.

Seminars and lectures given by Dr. Ross included: "Delayed Puberty, Primary Amenorrhea, and Sexual Infantilism", Second International Symposium on

Adolescent Medicine, Washington, D.C.; and "Normal Ovarian Function," IX Meeting of the International Study Group for Steroid Hormones, Rome, Italy.

Dr. Ross was invited to present The Zurkow Lecture, 'The Choice of the Ovulatory Follicle," Washington, D.C.; The Herbert M. Evans Memorial Lecture, "Ovulatory Follicles: The Chosen Few," University of California School of Medicine, San Francisco; The Winthrop Lecture, "Regulation of Ovulatory Function," American Fertility Society, Houston, Texas; and the Second James H. Leatham Lecture, 'Hormones and the Choice of the Ovulatory Follicle," College of Medicine and Dentistry of New Jersey, Piscataway.

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## NORMAL VOLUNTEER PROGRAM

### I. GENERAL STATEMENTS:

This year a series of events involving the care and use of normal volunteers for biomedical research has necessitated a complete review of the Normal Volunteer Program. Although there were several minor but significant incidents, the primary one was the death of a normal volunteer while participating on a study in the sleep lab. (See Section V, Special Incidents) This is the first time any serious mishap has occurred in the 27 year history of the program. An ad hoc committee has been formed to consider all aspects of the program including the motivation, screening, informed consent, patient care and reimbursement of normal volunteers.

In the past, contracts with organizations (college, universities, religious and community groups) sponsoring volunteers for biomedical research have been awarded on a non-competitive/sole source basis. With the recent restrictions placed on sole source contracts, and after much discussion regarding the ethical and practical issues of "bidding" to supply volunteers for our research, the decision was made that such procedures must be initiated. A "Sources Sought" synopsis has been placed in the "Commerce Daily Bulletin". Depending on the response, sponsoring agencies and contractual arrangements could alter considerably in the future.

Although we have been able to meet most of our investigators' requests for volunteers, we are experiencing difficulty in locating volunteers to participate on the more demanding protocols. Traditionally volunteers have been reimbursed only for their time, but plans are being considered to include some small additional reimbursement commensurate with the level of inconvenience or discomfort involved.

Another factor influencing the program this year has been the increased awareness by the general public to the adverse affects of radiation, carcinogenic substances, mood-altering drugs, etc. As a result, a stronger educational program has been developed for volunteers. Seminars are being conducted in such areas as radiation safety, bioethics, and informed consent to alleviate any fear as to the safety of our research. Also, a detailed list of the various activities on which volunteers can expect to participate has been compiled and each activity discussed with applicants during the personal interview. All effort is being made to help the applicant understand what to expect before volunteering.

The energy crisis has affected the program. Staff travel for interview sessions at the various colleges takes considerably more time due to fewer available flights and connections. The cost, and sometimes limited supply of gasoline, has created more expense for volunteers coming to the NIH.

In spite of the above difficulties the basic needs for volunteers by the research investigators have been met. Most volunteers agreed to all studies presented to them and performed with integrity, responsibility and good sportsmanship. Our contracting agencies continued to support our program and to encourage their members to participate. Three new organizations have contracted to provide volunteers for both inpatient and outpatient programs. The medical, nursing and administrative staff at the Clinical Center are continuing efforts to improve communication with and understanding of the volunteers and the difficulties these healthy young people face living in a hospital and participating in uncomfortable and demanding studies. A list of resource personnel has been made available to volunteers should problems arise for which they need guidance or advice. And the various Institutes are supporting the "career assignment" aspect of the program, affording the students a real learning experience. The benefits from this portion of the program are recognized as a major motivation for students' participation, as a purposeful activity during their stay at the Clinical Center, and as developing in these young people an increasing interest in biomedical research.

The outlook for next year indicates positive changes in screening procedures, closer monitoring of volunteers, further follow-up evaluation of their experiences, and a more flexible and equitable reimbursement plan. The development of educational programs to better inform volunteers of their role in biomedical research should create an even more responsible participant. These factors along with the continuing active and enthusiastic support of our sponsors along with that of current and past volunteers should strengthen the effectiveness of the total program.

## II. INPATIENT PROGRAM

The overall inpatient program remained relatively consistent with past years. The daily census ranged from 45-60 volunteers, representing about 15% of the total Clinical Center inpatient census. The same eight institutes continue to use inpatient volunteers with fluctuations based on the demands of the protocols. Some decrease in the projected need for volunteers toward the end of the year was due to the limited bed space available during reconstruction at the Clinical Center. Statistically, the number of inpatient volunteers decreased from that of last year, but the total number of days and the average daily stay increased. Note the following table:

| | No. of Vols. | Total No. Days | Average Days Per Volunteer |
|---|---|---|---|
| F.Y. 1979 | 433 | 16,701 | 38.57 |
| F.Y. 1980 | 372 | 18,100 | 48.66 |
| | 61 less | 1,399 more | 10.09 more |

Compared with last year, the total cost of the inpatient program increased by approximately 12%. This was due both to the increase in travel costs and the additional inpatient days.

| Fiscal Year | | Expenditures |
|---|---|---|
| 1980 | | $319,191.00 |
| 1979 | | - 283,773.00 |
| | Increase | $ 35,418.00 |

## III. OUTPATIENT and OFF-SITE PROGRAMS

The outpatient and off-site programs also vary from year to year depending on the needs of the specific research projects being conducted. Both NCI and NICHD used considerably fewer volunteers on an outpatient basis this year, while NIMH almost doubled the number of clinic visits and total hours. However, there was a substantial drop in the clinic visits for NIMH toward the end of the year with the closing of the sleep lab. The total number of clinic visits increased this year by 13% while the total hours increased by 62%. The total cost of the outpatient program also increased by 62%. Note the following table:

PER CLINIC VISITS

| | Visits | Total Hours | Expenditures |
|---|---|---|---|
| F.Y. 1980 | 3,726 | 17,906 | $134,575.00 |
| F.Y. 1979 | 3,307 | 11,020 | 82,937.00 |
| Increase | 419 | 6,886 | $ 51,680.00 |

The number of off-site visits and total hours doubled this year. NIMH was the only Institute using this resource. The studies mainly involved infant and child development and family interaction.

OFF-SITE VISITS

| | Visits | Total Hours | Expenditures |
|---|---|---|---|
| F.Y. 1980 | 3,987 | 8,596 | $40,053.50 |
| F.Y. 1979 | 2,838 | 5,527 | $24,509.00 |
| Increase | 1,149 | 3,069 | $15,544.50 |

## IV. VOLUNTEER RESOURCES

Contracting resources have actively supported our program through the year and have met most of our volunteer needs. Three new contracts have been written. One contract (Green Acres School) has been terminated because the study involving this group was completed. New contracts with East Carolina University and Sonoma State University, California, will provide inpatient volunteers and the contract with the Mt. Airy Ward of the Mormon Church will provide short term inpatient and outpatient volunteers. One college previously interested declined a contract due to concern over legal responsibility should harm or injury occur to a volunteer. Although our present contracts now number

23 (14 resources for long term inpatient volunteers and 9 resources for short term, OPD and Off-site volunteers). This may change with the new restrictions on non-competitive or sole source contracts. Responses to the "Sources Sought" have not been received as yet.

There have been several changes in liaison personnel at our various resources requiring more staff time orienting representatives unfamiliar with our program. Former volunteers continue to be enthusiastic "recruiters" as they return to campus and relate their experiences. More sponsors are sending representatives to the Clinical Center to observe their students and this has increased confidence in the program and awareness of the educational advantages offered students.

Two problem areas have continued this year. One is the difficulty obtaining volunteers for more demanding studies such as metabolic diets, mood altering drugs, lumbar punctures, etc. Also, it is difficult to locate volunteers between the ages of 35 and 55 years who can afford to volunteer their time. Several investigators, particularly in NIMH, need as controls the healthy, well-adjusted, successful individual. Adjustment in reimbursement rates to compensate for inconvenience and discomfort as well as time may attract volunteers for these types of studies. Reimbursement for travel costs may also have to be considered for the OPD volunteers as energy costs continue to rise.

## V. SPECIAL INCIDENTS

Of utmost concern has been the death of a "normal volunteer" while participating on a study in the sleep lab. The volunteer had not informed the investigator of her previous medical history. Her pre-screening (physical and psychological) did not indicate any abnormality. Thorough investigation showed her death was not attributable to the study. However, an in-depth review of the program is now underway and although present guidelines have been shown to be effective toward the protection of human subjects, additional guidelines for screening, patient care, informed consent and follow-up on volunteers will be required.

Several other incidents occurred during the year pointing out the need for closer attention to and responsibility in the use of volunteers.

1. One volunteer developed high blood pressure after an 8-day HCG infusion study. It is doubtful the study caused this, but it did leave a question in the volunteers' minds.

2. Another volunteer received a shock to his eye during an Iontophoresis. He lost vision in his eye for about 24 hours and then his vision returned to normal.

3. Several volunteers developed a higher radioactive thyroid count than expected due to a change in iodine dosage in pharmacy. Thyroi

activity was being monitored and all were within safe limits.

4. One volunteer was discharged after his PPD test was read incorrectly. The family requested a second test which proved negative and he was readmitted to another Institute.

5. A volunteer admitted in September was notified in November that he had hepatitis B. No thorough follow-up was made of tests conducted during his admission physical and he was placed on a study for which one of the risks noted is the possibility of transmitting a hepatitis virus. Only after completing the study was he advised that his liver levels had been elevated in October and that he must have been exposed to hepatitis B long before the study took place.

6. A female volunteer participating on a mood altering study was being monitored by another male volunteer with no medical or nursing staff present. She accused the male volunteer of making "sexual advances". There were no witnesses and no proof as to whether this was true or not. A satisfactory solution was developed, but it was a very difficult and sensitive issue.

7. Another volunteer felt threatened with discharge when he refused to participate on a study involving radioactive isotopes. He then advised the other volunteers of his fears of radiation and the possibility of his discharge with the result that general meetings were held with the volunteers to discuss radiation safety, right to refuse studies, and the commitment and responsibility of each volunteer.

8. Recently a volunteer was administered five times the amount of a hormone as prescribed in the protocol. Although this was not a dangerous amount it indicated to the volunteers a laxity inconsistent with good patient care and research.

9. And other volunteers have complained that more blood is being drawn than was expected or allowed.

Although the tabulation and analysis have not been completed on the volunteers' responses to the "Normal Volunteer Program Evaluation" form devised by Dr. John Fletcher, the same complaints as those in past years were noted:

- lack of consideration by medical, nursing and nutrition staff.
- being rushed and not given complete information by doctors obtaining informed consent.
- additional demands added after the study has begun.
- inequality of demands made on volunteers from one study to another or one Institute to another.
- difficulties of living on a mental health unit.

Another request volunteers make year after year is for an area where they can gather together without disturbing patients and staff. Hopefully a lounge area can be located for them when the ACRF is completed.

One more incident should be noted. A volunteer received a scalp laceration while on pass from the Clinical Center. After receiving emergency treatment at Georgetown University Hospital she returned to the Clinical Center. Due to the development of infection she was transferred to patient status for further diagnostic work-up and treatment. Her condition improved and she was discharged in early July.

## VI. CAREER DEVELOPMENT

The career development aspect of the program continues as a major motivating force for colleges, universities and their students to participate. Student volunteers eagerly seek a career assignment in their field of study and make every effort to gain a maximum learning experience. Most students are majoring in the pre-medical and affiliated sciences and health fields although we also have a few students interested in other areas such as computer programming, art therapy, hospital administration, etc. All volunteers were placed in appropriate assignments and their preceptors were pleased with these bright, inquisitive, highly motivated young people and their new ideas and fresh approach to research. The valuable experience the volunteer receives is readily acknowledged by the students and their respective colleges and this stimulates interest for future applicants.

There was some difficulty this summer locating suitable career assignments due to many investigators leaving NIH and to the number of "summer interns" working in the laboratories. The various Institutes will be contacted to open up new assignments for our volunteers. I expect the same enthusiastic support and cooperation from the Institutes and their scientists as we have had in the past.

## VII. AGE RANGE

The inpatient volunteers ranged in age from 6 to 69 years with college age students, 19 to 22 years, constituting the largest group. Most volunteers remaining in the Clinical Center for an extended period of time (3 to 4 months) were college age students. However, they comprised only about 60% of the total inpatient group. The other 40% were recruited from local community resources to participate on short term inpatient studies. There is a need for older normal volunteers between 35 and 55 years of age who are healthy, well-adjusted, productive people. These volunteers are most difficult to find as they cannot afford the time our studies often demand.

## VIII. SEX RATIO

The percentage of male and female volunteers is dictated primarily by the nature of the research studies. We have been able to meet the requests of the investigators for both men and women, but, again this year, many more women than men have applied. Of the 372 volunteers participating this year, 171 were men (46%) and 201 were women (54%).

## IX. COST OF VOLUNTEER PROGRAM

This fiscal year reflects a 25% increase in the total cost for volunteer services from that of last year. Costs are computed on a per diem and per capita (travel expense) basis for inpatient services and on an hourly basis for OPD and Off-Site services. The following shows this increase.

| | Total Expenditures |
|---|---|
| F.Y. 1980 | $493,819.50 |
| F.Y. 1979 | - 390,833.00 |
| Increase | $102,986.50 |

This increase is due to rising travel expenses for inpatients, and to an increase in the number of inpatient days and clinic and off-site visits and total hours.

## CHART # 1

### TOTAL ESTIMATED* EXPENDITURES BY AGENCY FOR FISCAL YEAR 1980

| AGENCY | AMOUNT |
|---|---|
| Alderson-Broaddus College | $ 3,330.00 |
| California State University, Chico | 65,844.00 |
| Church of the Brethren General Board | 32,877.00 |
| Church of Jesus Christ of L.D.S., (Mormon) Frederick Ward | 3,630.00 |
| Church of Jesus Christ of L.D.S., (Mormon) Gaithersburg Ward | 3,138.50 |
| Church of Jesus Christ of L.D.S., (Mormon) Kensington Ward | 1,449.25 |
| Church of Jesus Christ of L.D.S., (Mormon) Mt. Airy | 2,024.25 |
| Church of Jesus Christ of L.D.S., (Mormon) Rock Creek Ward | 4,860.00 |
| Davidson College | 5,888.00 |
| East Carolina University | 918.00 |
| Gustavus Adolphus College | 23,631.00 |
| Indiana State University, Terre Haute | 5,169.00 |
| Kalamazoo College | 24,521.00 |
| Keuka College | 12,926.00 |
| Lions Club International | 3,515.00 |
| Mental Health Association of Montgomery County | 182,600.00 |
| Montgomery College | 5,695.00 |
| Ohio State University | 4,928.00 |
| Pennsylvania State University | 12,993.00 |
| University of California, Davis | 38,089.00 |
| University of California, Santa Cruz | 30,672.00 |
| Warner Memorial Presbyterian Church | 5,640.50 |
| Wittenberg University | 19,481.00 |
| | $493,819.50 |

* July, August, September 1980 estimated

## CHART # 2

## TOTAL ESTIMATED* EXPENDITURES BY INSTITUTE FOR FISCAL YEAR 1980

| INSTITUTE | AMOUNT |
|---|---|
| NCI | $ 20,496.50 |
| NIAID | 59,815.00 |
| NIAMDD | 36,008.00 |
| NHLBI | 64,250.50 |
| NICHD | 55,755.75 |
| NIMH | 229,734.75 |
| NINCDS | 6,377.50 |
| NEI | 17,640.75 |
| NIDR | 3,740.75 |
|  | $ 493,819.50 |

* July, August, September 1980 estimated

CHART # 3

## NUMBER OF VOLUNTEERS, TOTAL DAYS & EXPENDITURES (Inpatient)*

October 1, 1979 to September 30, 1980

### BY INSTITUTE

| INSTITUTE | VOLUNTEERS | TOTAL DAYS | AMOUNT |
|---|---|---|---|
| NCI | 12 | 975 | $ 17,084.00 |
| NEI | 20 | 855 | 15,340.00 |
| NIAID | 49 | 3280 | 59,161.00 |
| NIAMDD | 36 | 2022 | 36,008.00 |
| NHLBI | 50 | 3466 | 64,196.00 |
| NICHD | 43 | 3577 | 50,576.00 |
| NIMH | 149 | 3889 | 75,976.00 |
| NINCDS | 13 | 36 | 850.00 |
|  | 372 | 18,100 | $ 319,191.00 |

### BY AGENCY

| AGENCY | VOLUNTEERS | TOTAL DAYS | AMOUNT |
|---|---|---|---|
| Alderson-Broaddus College | 3 | 230 | $ 3,330.00 |
| California State University, Chico | 30 | 3411 | 65,844.00 |
| Church of the Brethren General Board | 34 | 2009 | 32,877.00 |
| Church of L.D.S., Gaithersburg | 3 | 4 | 79.00 |
| Church of L.D.S., Kensington | 6 | 10 | 278.00 |
| Church of L.D.S., Mt. Airy | 1 | 1 | 49.00 |
| Church of L.D.S., Rock Creek | 2 | 8 | 158.00 |
| Davidson College | 8 | 383 | 5,888.00 |
| East Carolina University | 2 | 43 | 918.00 |
| Gustavus Adolphus College | 19 | 1423 | 23,631.00 |
| Indiana State University, Terre Haute | 7 | 297 | 5,169.00 |
| Kalamazoo College | 22 | 1347 | 24,521.00 |
| Keuka College | 20 | 679 | 12,926.00 |
| Mental Health Assoc., Mont. Co. | 122 | 2297 | 37,309.00 |
| Montgomery College | - | - | - |
| Ohio State University | 6 | 283 | 4,928.00 |
| Pennsylvania State University | 14 | 897 | 12,993.00 |
| University of California, Davis | 30 | 2054 | 38,089.00 |
| Univ. of Calif, Santa Cruz | 22 | 1503 | 30,672.00 |
| Warner Memorial Presbyterian Church | 1 | 2 | 51.00 |
| Wittenberg University | 20 | 1219 | 19,481.00 |
|  | 372 | 18,100 | $ 319,191.00 |

*July, August, and September 1980 estimated

CHART # 4

ESTIMATED* OUTPATIENT REPORT FOR PERIOD OCTOBER 1, 1979-SEPTEMBER 30,1980

BY AGENCY

| AGENCY | TOTAL VISITS | TOTAL HOURS | AMOUNT |
|---|---|---|---|
| Church of L.D.S., Frederick | 80 | 475 | $ 3,630.00 |
| Church of L.D.S., Gaithersburg | 119 | 248 | 2,261.50 |
| Church of L.D.S., Kensington | 56 | 136 | 1,171.25 |
| Church of L.D.S., Mt. Airy | 71 | 143 | 1,975.25 |
| Church of L.D.S., Rock Creek | 295 | 464 | 4,702.00 |
| Mental Health Assoc., of Mont. Co. | 2,942 | 16,049 | 117,429.50 |
| Montgomery College | 142 | 348 | 3,011.00 |
| Warner Memorial Presby. Church | 21 | 43 | 394.50 |
| | 3,726 | 17,906 | $134,575.00 |

BY INSTITUTE

| INSTITUTE | TOTAL VISITS | TOTAL HOURS | AMOUNT |
|---|---|---|---|
| NCI | 273 | 273 | $ 3,412.50 |
| NIAID | 12 | 96 | 654.00 |
| NIAMDD | - | - | - |
| NHLBI | 1 | 8 | 54.50 |
| NICHD | 327 | 446 | 5,179.75 |
| NIMH | 2,568 | 15,780 | 113,705.25 |
| NINCDS | 254 | 646 | 5,527.50 |
| NEI | 72 | 293 | 2,300.75 |
| NIDR | 219 | 364 | 3,740.75 |
| | 3,726 | 17,906 | $134,575.00 |

* July, August, & September 1980 estimated

## CHART # 5

## ESTIMATED* OFF-SITE REPORT FOR PERIOD OCTOBER 1, 1979 to SEPTEMBER 30, 1980

### BY AGENCY

| AGENCY | TOTAL VISITS | TOTALS HOURS | AMOUNT |
|---|---|---|---|
| Church of L.D.S., Gaithersburg | 84 | 168 | $ 798.00 |
| Lions International | 482 | 660 | 3,515.00 |
| Mental Health Assoc., Montgomery Co. | 2,571 | 6,124 | 27,861.50 |
| Montgomery College | 305 | 549 | 2,684.00 |
| Warner Memorial Presbyterian Church | 545 | 1,095 | 5,195.00 |
| | 3,987 | 8,596 | $ 40,053.50 |

### BY INSTITUTE

| INSTITUTE | TOTAL VISITS | TOTAL HOURS | AMOUNT |
|---|---|---|---|
| NIMH | 3,987 | 8,596 | $ 40,053.50 |

* July, August, & September 1980 estimated

## Epidemiology Service

## I. DEPARTMENT MISSIONS AND GOALS

The mission of the Epidemiology Service is threefold:

1. To prevent the transmission of infection between patients and between patients and staff.

2. To limit such infections present in the patient/personnel population by instituting appropriate effective precautionary measures.

3. To serve the Clinical Center staff in their efforts to reduce the potential risk of infection to all Clinical Center patients and personnel.

## II. DEPARTMENT ACTIVITIES

### Personnel and Budget

The Epidemiology Service staff consists of a physician, two full-time nurse epidemiologists and a part-time secretary.

The Epidemiology Service has been working with a full staff since October, 1979. The focus of the Epidemiology Service for the first full year of operation has necessarily been on establishing a foundation on which future progress in both routine surveillance and research in the field of nosocomial infection can be done.

The Epidemiology Service has seen its major expenditures for FY 1980 in the areas of purchase of relevant resource materials, various educational aids (i.e., slides, photographs, and poster boards on the subject of waste management in the Clinical Center) as well as limited travel to and from educational sessions.

## III. MAJOR PROGRESS

1. The Epidemiology Service developed and implemented a comprehensive biological monitoring (spore strips) of all sterilizers in the Clinical Center and autoclaves used for patient related items.

2. The Epidemiology Service investigated a problem identified with 8 of 9 steam sterilizers in the three operating suites. Spore strips from these 8 sterilizers were found to be positive on the same day.

   Required communication/collaboration was established with the Surgical Services Department, Engineering Section, surgeons from NEI, NCI, NHLBI, NINCDS, an Ear, Nose and Throat consultant and an AMSCO representative. After thorough investigation no firm

conclusions as to the cause were reached. With cooperation from all departments listed precautions were taken so that no patients were placed at risk of exposure to items which may not have been adequately sterilized.

3. The first Clinical Center Infection Control Manual was developed by the Epidemiology Service. This comprehensive manual includes all Clinical Center policies and procedures related to infection prevention and control. Each patient and employee-related service or department submitted their relevant procedures for compilation and annual review by the Hospital Infections Committee.

4. The Epidemiology Service coordinated varicella titer surveillance of susceptible personnel exposed to patients with varicella.

5. A survey was conducted among a small group of nursing personnel to determine potential transmission of Herpes simplex II infection from patient to staff.

6. Epidemiological investigation was conducted on the following clusters of infection:

   a. There was an outbreak of Staphylococcus aureus wound infections on the NCI surgical consult service in the Fall of 1979. After identification of all affected patients (total of 5), and review of numerous possible sources of the infections, it was found that one patient care giver was involved in the care of all five patients. Nasal cultures from this individual were positive for the causative organism, Staphylococcus aureus. After appropriate therapy was instituted, no new cases were identified.
   b. A total of five cases of mediastinitis were identified between the months of November 1979 and June 1980 on the NHBLI surgical service. The causative agent varied from patient to patient.

      An exhaustive investigation by the Epidemiology Service was done including review of the following areas:

      Operating room air handling system;
      Operating room personnel present at time of surgery;
      Sterilization process of operating room items/instruments;
      Operating room procedures/practices;
      Pre-and postoperative care of cardiac surgical patients;
      6W surgical unit personnel.

Although no clear source was identified, emphasis was placed on those practices and procedures which can contribute to an increased infection rate. A list of regulations which are intended to minimize the incidence of post surgical wound infection was developed by the Epidemiology Service in collaboration with members of the surgical and anesthesia staff. These

regulations are now included in the Policy and Communications Bulletin dated June 20, 1980. In addition, numerous meetings and educational sessions have been held with the surgical and nursing staff. Ongoing surveillance of patients undergoing cardiac surgery continues at this time. In March 1980, the NCI surgical consult service experienced a small case cluster of Staphylococcus aureus wound infections. Three patients developed wound infections postoperatively - each Staphylococcus aureus isolate was different by phage typing. However, nasal cultures from two of the four surgeons grew Staphylococcus aureus. The organism isolated from surgeon A matched the organism from case #1 while the organism from surgeon B matched that of case #2. Therapy was instituted and no new cases were identified.

Numerous individual patient and/or employee epidemiological investigations were done for the following problems: tuberculosis, hepatitis A, Legionnaire's Disease, chicken pox (Varicella), herpes zoster, and nosocomial bacteremia in a normal volunteer.

7. The Epidemiology Service developed and distributed a guide to waste disposal in the Clinical Center patient care areas.
8. The use of a surgical progress note was instituted for the purpose of identifying surgical case classification.

## Training

To achieve our goal of infection prevention, the Epidemiology Service has dedicated much time and effort in providing educational sessions to many Clinical Center employees. The following are some of the educational programs conducted by the Epidemiology Service:

1. Bimonthly orientation to all new Clinical Center employees.
2. Comprehensive yearly mandatory review for nurses conducted at least once a month.
3. Orientation to Clinical Associates on the NIAID service.
4. Inservices to the following Clinical Center departments/services were conducted during FY 1980: Nursing, Outpatient Department, Central Sterile Supply, Pharmacy, Clinical Pathology, Supervisory Training group, 14th floor playroom staff, Occupational Medicine Services, and Surgical Services.

5. As an additional method of educating and reviewing with patients care staff, rounds were conducted in all three intensive care units to assist the nurses in identifying improved methods of infection prevention.
6. Formal educational sessions lasting one hour each, on topics of particular interest and relevance to Clinical Center employees. The first session on Hepatitis B was given March 7, 1980. The second session on the topic of Varicella Zoster Virus Infections will be given July 29, 1980.

## Research

Since September 1979 the Epidemiology staff has been collaborating

with Dr. Murray Brennan of the NCI Surgery Branch in an effort to study catheter-related sepsis among patients receiving Total Parenteral Nutrition (TPN). Having collated and analyzed the data generated from the past several years, it has been decided to develop criteria for diagnosing catheter-related sepsis and instituting a protocol.

A short-term infection surveillance study was conducted by the Epidemiology staff with the assistance of Dr. Phillip Pizzo, NCI Pediatric Oncology Branch. Comparison was made between patients identified as infected by traditional microbiological surveillance and infected patients identified by alternative methods.

## IV. FUTURE OBJECTIVES

The Epidemiology Service will continue to direct its activities toward the following goals:

1. To continue an ongoing collaboration with the Total Parenteral Nutrition team (TPN) in answering specific research questions related to sepsis in the TPN patient.
2. To initiate a Hepatitis B surface antigen surveillance program among high risk Clinical Center employees.
3. To conduct infection prevention rounds in the intensive care nursing units, i.e., 10D, 10N and 6W.
4. To continue the Epidemiology Service educational programs on relevant infection prevention/control topics for the Clinical Center employees.
5. To evaluate compliance with the surgical wound classification progress note and subsequently determine surgical infection rates using data gathered from these progress notes.
6. To develop and conduct a brief orientation program (session) for newly arriving Clinical Associates.
7. To pan and initiate a systematic review of Clinical Center Infection Control Manual policies and procedures.
8. To collaborate with the Microbiology Department in the preparation of current antibiotic susceptibility patterns.
9. To continue to assess the potential for computer access in order to assist in ongoing Clinical Center infection surveillance and infection control research.
10. To evaluate new methods of collecting nosocomial infection surveillance data.

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# ANNUAL REPORT 1979 - 1980
# ANESTHESIOLOGY

## I. DEPARTMENT MISSIONS AND GOALS

The Anesthesiology Section, a division of Georgetown University Department of Anesthesia, is responsible for the clinical care of all patients requiring anesthesia and related clinical and research support services at the Clinical Center, the teaching of medical students, residents, postgraduate physicians and other health personnel, and the development and continuation of a varied research program.

The missions of the department are:

1) To provide all patients at the Clinical Center with a trained anesthetist and medical consultant in the areas of surgical anesthesia, pain therapy, resuscitation, and critical care.
2) To provide professional support to other divisions of the Clinical Center and the various Institutes in their investigational programs.
3) To initiate primary clinical investigations when opportune and appropriate.
4) To provide a teaching program for postgraduate physicians, residents, medical students, and other health personnel in the principles and clinical practice of anesthesia.
5) To participate in and expand the continuing medical education program of the Clinical Center.

## II. DEPARTMENT ACTIVITIES

### CLINICAL

During the past twelve months, anesthesia and/or supportive treatment has been provided in 1875 instances, representing 1347 surgical operations, 416 diagnostic procedures, 57 nerve blocks and 55 miscellaneous procedures. Of these 156 were emergency procedures and 212 were open heart procedures requiring the techniques of extracorporeal circulation. There were approximately 250 cancellations and 345 add-on procedures.

The accompanying tables indicate the distribution of patients according to sponsoring Institute and responsible surgical service (Table I); the distribution of anesthesia time by responsible surgical service (Table II); and the distribution of patients by anesthetizing location (Table III).

Analysis of these statistics reveals that the average length of a case is approximately 3.5 hours. Anesthesia support

### TABLE I: DISTRIBUTION OF PATIENTS ACCORDING TO SPONSORING INSTITUTE AND RESPONSIBLE SURGICAL SERVICE-1980

| SPONSORING INSTITUTE | DISTRIBUTION OF PATIENTS | | | |
|---|---|---|---|---|
| | SPONSORING INSTITUTE | | RESPONSIBLE SURGICAL SERVICE | |
| | # | % | # | % |
| NCI | 967 | 54.8 | 1205 | 68.3 |
| NHLBI | 393 | 22.3 | 384 | 21.8 |
| NINCDS | 102 | 5.8 | 100 | 5.7 |
| NEI | 24 | 1.4 | 24 | 1.4 |
| NIDR | 11 | .6 | 11 | .6 |
| NICHD | 31 | 1.8 | 2 | .1 |
| NIAMDD | 125 | 7.1 | 6 | .3 |
| NIAID | 67 | 3.8 | --- | --- |
| NIMH | 43 | 2.4 | 31 | 1.8 |
| TOTAL | 1763 | 100.0 | 1763 | 100.0 |

### TABLE II: DISTRIBUTION OF ANESTHESIA TIME BY RESPONSIBLE SURGICAL SERVICE-1980

| RESPONSIBLE SURGICAL SERVICE | TOTAL NUMBER CASES | AS A % OF THE TOTAL | LESS THAN 3 HOURS | | 3 TO -5 HOURS | | 5 HOURS AND OVER | |
|---|---|---|---|---|---|---|---|---|
| | | | # | % | # | % | # | % |
| NCI | 1205 | 68.3 | 599 | 49.7 | 351 | 29.1 | 252 | 20.9 |
| NHLBI | 384 | 21.8 | 130 | 33.8 | 104 | 27.1 | 150 | 39.1 |
| NINCDS | 100 | 5.7 | 32 | 32.0 | 30 | 30.0 | 38 | 38.0 |
| NEI | 24 | 1.4 | 23 | 95.8 | --- | ---- | 1 | 4.2 |
| NIDR | 11 | .6 | 9 | 81.8 | 1 | 9.1 | 1 | 9.1 |
| NICHD | 2 | .1 | 2 | 100.0 | --- | ---- | --- | ---- |
| NIMH | 31 | 1.8 | 30 | 96.8 | 1 | 3.2 | --- | ---- |
| NIAMDD | 6 | .3 | 6 | 100.0 | --- | ---- | --- | ---- |
| TOTAL | 1763 | 100.0 | 831 | 47.1 | 487 | 27.6 | 442 | 25.1 |

### TABLE III: DISTRIBUTION OF PATIENTS BY ANESTHETIZING LOCATION

| LOCATION | Patients | |
|---|---|---|
| | 1980 | 1979 |
| 1. Main Surgical Suite-Bldg 10 | 1158* | 1024 |
| 2. X-Ray Dept. -Bldg 10 | 49 | ** |
| 3. Cardiac Cath Lab-Bldg 10 | 28 | 7 |
| 4. Surgical Suite-Bldg 10A - Heart | 320 | 360 |
| 5. Surgical Suite-Bldg 10A - Neuro | 106 | 89 |
| 6. Cath Lab-Bldg 10A | 19 | 5 |
| 7. Dental | 3 | 5 |
| 8. Hyperthermia-Bldg 10-13th Fl | 74 | 96 |
| 9. Electroconvulsive Therapy 10-4W | 23 | 42 |
| 10. Radiation Therapy | 30 | ** |
| 11. Units | 10 | ** |
| (Excluding nerve blocks = 1763) SUBTOTAL | 1820 | 1628 |
| 12. A. Emergency Intubation | 12 | ** |
| B. Resuscitation | 12 | ** |
| C. Consults | 25 | ** |
| D. Other Miscellaneous | 6 | 39 |
| *Includes 57 nerve blocks TOTAL | 1875 | 1667 |

**Not identified in statistics

for the Hyperthermia Project of the NCI was an integral part of the Department's case load. There were 74 hyperthermia cases during the past year with an average length of 6 - 7 hours per case.

The Recovery Room, in its second full year of operation, admitted an average of 6-7 patients per day. Approximately 20% of all blood gases were performed by Recovery Room personnel. In addition, the Recovery Room has expanded its coverage to outpatient pediatric radiotherapy patients undergoing anesthesia on the B3 level of the Clinical Center and to the neurosurgery patients recovering on 5 West. In summary, there were 64 patients reacted by Recovery Room personnel in an area other than the Recovery Room. Also the Recovery Room is used for diagnostic and therapeutic blocks that arise as part of our consultative services in pain management. Utilizing this facility reduces the workload on the Operating Room staff. Utilization of the Recovery Room and Recovery Room personnel continues to exceed anticipated goals.

## TEACHING

The second major activity of the Anesthesia Section is the teaching of medical students, residents, and postgraduate physicians. The Department again offered two week electives throughout the year to third year medical students in the Georgetown University Surgery Clerkship. Forty-eight students participated in the two week elective at the Clinical Center. The basic format of the course includes a clinical demonstration, faculty tutorial, and a self-teach audiovisual program. Participation in the didactic sessions has been extended to other students involved in the Clinical Center Preceptorship Program.

As part of the Department's Residency Program, rotations were provided at the Clinical Center for senior residents in cardiac anesthesia, major cancer surgery, research and pulmonary medicine. Residents who complete a rotation at the Clinical Center are expected to prepare a paper for presentation before a national audience or a publication for a peer review journal.

The Department has greatly expanded its teaching of cardiopulmonary resuscitation at the Clinical Center. The staff now conducts ongoing courses in Basic Cardiac Life Support in conjunction with Occupational Medical Services (OMS). In addition, courses in Advanced Cardiac Life Support are also conducted as the need for additional ACLS providers is identified by the Clinical Directors of the various Institutes serving within the Clinical Center.

## RESEARCH

The division continued to provide professional support for the various Institutes and divisions of the Clinical Center conducting clinical research. Formally the Department was involved in the following protocols in the last twelve months:

1) Effects of Chronic Electrical Stimulation of the Brain and Narcotic Analgesics on Human Responses to Noxious and Non-noxious Stimuli: Clinical and Experimental Evaluations (NIDR).
2) Effect on Whole Body Hyperthermia Combined with Adriamycin in Patients with Metastatic Sarcoma and Other Cancers (NCI).
3) Phase I - II Trial of Hyperthermia and Methyl CCNU in Malignant Melanoma (NCI).
4) A phase I Trial of Systemic Hyperthermia and DTIC in Malignant Melanoma (NCI).
5) Post-Thoracotomy Pain Study (NCI) - study concluded.
6) Elucidation of Basic Mechanisms of Taste: Transduction by Studying the Effects of Topically Applied Neuropharmacologically Active Drugs on Taste Acuity in Normal Human Beings (NIAID) - study concluded.
7) Use of Somatosensory Evoked Responses in Assessing Analgesia During General Anesthesia (NIMH, NCI).
8) Evaluation of Techniques for Peripheral Nerve Transection and Handling During Amputation and Their Relationship to Phantom Limb Phenomena (NCI).

## III. MAJOR PROGRESS IN RESEARCH, SERVICES, TRAINING, AND DEVELOPMENT.

To date all members of the Anesthesia Section are certified in Basic Cardiac Life Support and approximately 1/3 of the Department are certified in Advanced Cardiac Life Support. The goal is to have all members of the Department possess current ACLS certification. This has been made possible by establishing a teaching cadre within the Department to service both Department and Clinical Center needs. Presently we have four R.N.'s certified as BCLS Instructors, 2 R.N.'s certified as ACLS Instructors and one physician who is both an ACLS Instructor and Course Director. The Department conducts frequent BCLS courses and is presently arranging its second ACLS course for Clinical Center personnel this year.

In its endeavor to expand continuing medical education, the Department again co-sponsored the Annual Chesapeake Bay Anesthesia Conference in May 1980, in conjunction with other academic anesthesia groups. The meeting was attended by approximately 200 anesthetists and anesthesiologists from the mid-Atlantic area.

The Department hosted Edmond I. Eger, II, M.D., who visited our Department as the William N. Creasy Visiting Professor of

Clinical Pharmacology, sponsored by the Burroughs Wellcome Fund. Dr. Eger is a Professor of Anesthesia at the University of California, San Francisco, and is the Vice Chairman for Research. While at NIH he conducted several seminars with members of our Department and with the Chemical Pharmacology Laboratory of the NHLBI.

An ongoing audit system was established during the year to provide information on the quality of clinical care and to ensure that once problems were identified they were remedied. To this end, we established a nurse observer who surveys the anesthetic record and also visits the patient postoperatively. She has been trained to observe for specific perioperative incidents and report them to the Chief of the Department who then decides upon the action necessary. These ongoing audits are submitted to both the Medical Audit Committee and the Quality Assurance Committee. In addition, one of our nurse observers serves on the Medical Audit Comittee.

The Department displayed two scientific exhibits within the last year at major national and international meetings. At the 54th Congress of the International Anesthesia Research Society, the Department displayed an exhibit on "Intraoperative Application of Mass Spectrometry in Anesthesia". This exhibit was also shown at the New York Postgraduate Assembly in New York City in December, 1979. The exhibit on "Anesthesiology in Whole Body Hyperthermia" was displayed at the Annual Meeting of the Southern Medical Association in Las Vegas, Nevada, on November 4-7, 1979.

The following papers were presented at national anesthesia meetings and/or published as a result of this work:

PRESENTATIONS

1) Kim YD, Lees DE, Lake CR et al: Hyperthermic alteration of regional sympathetic activity in anesthetized man. Presented at the Annual Meeting of the American Society of Anesthesiologists, San Francisco, CA, October 19-24, 1979

2) Lees DE, Kim YD, Macnamara TE: Pulmonary shunting with hyperthermia under anesthesia. Presented at the Annual Meeting of the American Society of Anesthesiologists, San Francisco, CA, October 19-24, 1979 (Poster)

3) Lees DE, Hanowell ST, Kennedy SF, et al: Celiac plexus block: diagnostic and therapeutic application in abdominal pain. Presented at the Annual Meeting of the Southern Medical Association, Las Vegas, Nevada, November 4-7, 1979

4) Lees DE, Kim YD, Macnamara TE: Noninvasive determination of core temperature under anesthesia. Presented at the Annual Meeting of the Southern Medical Association, Las Vegas, Nevada, November 4-7, 1979

5) Lees DE, Kim YD, Macnamara TE: Internal organ hypoxia during hyperthermic cancer therapy in humans. Presented at the Third International Symposium: Cancer Therapy by Hyperthermia, Drugs and Radiation, Fort Collins, Colorado, June 22-26, 1980 (Poster)

6) Park WY, Massengale M, Kim SI, Poon KC, Macnamara TE: Epidural analgesia level and the ageing. Presented at the 54th Congress of the International Anesthesia Research Society, Reno, Nevada, March 9-13, 1980

7) Park WY, Macnamara TE: Interaction of trimethaphan and pancuronium. Presented at the Annual Meeting of the Southern Society of Anesthesiologists, Walt Disney World, Florida, March 20-22, 1980

In addition, individual staff lectured at a variety of educational programs as follows:

Janice Clements, R.N.

Instructor, Basic Cardiac Life Support Course, CPR Center, NIH, April 10 & 17, May 6 & 16, 1980

Prasad L. Gadde, M.B.B.S.

Reflex Sympathetic Dystrophy, NCI Surgical Branch Conference, April 1, 1980

Susan Hanowell, M.D.

Basic CPR and endotracheal intubation. Cardiac Clinical Associates, Clinical Center, NIH, July 11, 1979

Basic CPR. Radiology Department, Clinical Center, NIH, July 21, 1979

Airway management, Radiology Department, Clinical Center, NIH, August 5, 1979

Faculty, Advanced Cardiac Life Support, Fairfax Hospital, April 8-9, 1980

Course Director, Advanced Cardiac Life Support Course, Georgetown University Hospital, May 20-21, 1980

David E. Lees, M.D.

Anesthesia for Chemo- and Radiotherapy, Second Annual Chesapeake Bay Area Anesthesia Conference, May 7-9, 1980

Barbara LoGrasso, R.N.

Crohn's Disease, Workshop on the Care of the Patient with Acute Gastrointestinal Disease, Georgetown University Hospital, October 19, 1979

Instructor, Basic Cardiac Life Support Course, CPR Center, NIH, May 6 & 16, 1980

Instructor and Course Coordinator, Advanced Cardiac Life Support Course, Georgetown University Hospital, May 20-21, 1980

Thomas E. Macnamara, M.B., Ch.B.

Whole Body Hyperthermia, Anesthesia Grand Rounds, The Mayo Clinic, May 14, 1980

Patrick Mansfield, M.D.

Preparation for Medical School, Virginia State University, October 10, 1979

Indications and Contra-indications of Intravenous Heparin, Surgical Nursing Section, Clinical Center, April 17, 1980

Judith Miller, R.N.

Instructor, Basic Cardiac Life Support Course, CPR Center, NIH, April 10 & 17, 1980

Eileen Pierce, R.N.

Instructor and Course Coordinator, Advanced Cardiac Life Support Course, Georgetown University Hospital, May 20-21, 1980

PUBLICATIONS

1) Dubois M: DSA system misleading. (Letter) Anesthesiology 52:101-102, 1980
2) Dubois M, Sato S, Lees DE, et al: Electroencephalographic changes during whole body hyperthermia in humans. EEG & Neurophysiol J (in press)

3) Dubois M, Lotze MT, Diamond WJ, Kim YD, Flye MW, Macnamara TE: Pulmonary shunting during leukoagglutinin induced noncardiac pulmonary edema. JAMA (in press)

4) Hanowell ST, Kennedy SF: Phantom tongue pain and causalgia: case presentation and treatment. Anesth Analg 58:436-438, 1979

5) Hanowell ST, Kennedy SF, Lees DE, et al: Celiac plexus block: diagnostic and therapeutic application in abdominal pain. South Med J (in press)

6) Hanowell S, Lees DE, Macnamara TE: Auriculotemporal syndrome after combined modality therapy for cancer. South Med J 72:1116-1117, 1979

7) Kim YD, Hittner KC, Lees DE, et al: Vasodilator correction of hypotension in the postoperative period. South Med J 72:1501-1502, 1979

8) Kim YD, Lake CR, Lees DE, et al: Hemodynamic and plasma catecholamine responses to hyperthermic cancer treatment in humans. Am J Physiol 237(5):H570-574, 1979

9) Kim YD, Lake CR, Lees DE, et al: Hyperthermic alteration of sympathetic activity. Anesthesiology 51:S127, 1979 (Abstract)

10) Lees DE: Liquid crystal thermometry. (Letter) Anesth Analg 58:351, 1979

11) Lees DE, Gadde PL, Macnamara TE: Malignant hyperthermia in association with Burkitt's lymphoma. Anesth Analg 59:514-515, 1980

12) Lees DE, Kim YD, Bull JM, et al: Anesthetic management of whole body hyperthermia for the treatment of cancer. Anesthesiology 52:418-428, 1980

13) Lees DE, Kim YD, Macnamara TE: Pulmonary shunting with hyperthermia under anesthesia. Anesthesiology 51:S385, 1979 (Abstract)

14) Lees DE, Kim YD, Macnamara TE: Noninvasive determination of core temperature under anesthesia. South Med J (in press)

15) Lees DE, Kim YD, Schuette WH, et al: Auscultatory confirmation of placement of esophageal temperature probe. Anesthesiology Review 6:35-38, 1979

16) Lees DE, Schuette WH: Microwave rewarming. (Letter) Anesth Analg 59:161, 1980

17) Park WH, Massengale M, Kim SI, Poon KC, Macnamara TE: Age and the spread of local anesthetic solutions in the epidural space. Anesth Analg (in press)

18) Park WY, Massengale M, Macnamara TE: Age, height, and speed of injection as factors determining caudal anesthetic level, and occurrence of severe hypertension. Anesthesiology 51:81-84, 1979

19) Schuette WH, Lees DE, Bull JM, et al: Regulation of core body temperature during whole body hyperthermia by esophageal temperature feedback. Medical and Biological Engineering and Computing (in press)

20) Thibault LE, Schuette WH, Lees DE: An instrument to determine the hemoglobin-oxygen equilibrium curve based on the calculataed diffusion of oxygen across a semi-permeable membrane. Medical and Biological Engineering and Computing (in press)

## IV. FUTURE OBJECTIVES

The principal objective of the Department continues to be the provision of appropriate anesthesia support and clinical care for patients within the Clinical Center. In particular, in the upcoming year Department efforts will be focused on the expansion and upgrading of the monitoring facilities within the various operating suites. An emphasis will be placed on computer applications to both improve the level of care and to expand the teaching possibilities at the Clinical Center.

PROJECT NUMBER (Do NOT use this space) | HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | Z01-CL-08001-01 ANES

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

A Phase I Trial of Systemic Hyperthermia and DTIC in Malignant Melanoma

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

|  |  |  |  |
|---|---|---|---|
| PI: | Joan M. Bull, M.D. | Senior Investigator | ROB, DCT, NCI |
| Other: | D.E. Lees, M.D. | Deputy Chief | ANES, CC |
|  | R. Smith, R.N. |  | Nursing, CC |
|  | W. Schuette | Chief, ACE | BEIB, DRS |
|  | J. Schwade, M.D. |  | ROB, DCT, NCI |
|  | J. Tepper, M.D. |  | ROB, DCT, NCI |

COOPERATING UNITS (if any)

NCI, CC, DRS

LAB/BRANCH

SECTION

Anesthesia Section

INSTITUTE AND LOCATION

Clinical Center, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS: 6 | PROFESSIONAL: 6 | OTHER:

CHECK APPROPRIATE BOX(ES)

☑ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The protocol involving DTIC and hyperthermia and the treatment of malignant melanoma follows phase I and phase II protocols studying the effect of BCNU in combination with hyperthermia for the treatment of melanoma. DTIC is a standard chemotherapeutic agent with activity against melanoma. It can be administered intravenously as a single bolus with repeat cycles every three to four weeks and myelosuppression is not cumulative in contrast to the nitrosoureas. In the design of this protocol a total of 10 patients will be studied starting initially with 600 mg/m$^2$ and progressing up to 1000 mg/m$^2$. In each case, the drug will be given in coincident with two hours of hyperthermia to 41.8 C. The hyperthermia with DTIC will be repeated every three to four weeks provided the patient does not show disease progression on protocol.

PROJECT NUMBER (Do NOT use this space)

HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NOTICE OF
INTRAMURAL RESEARCH PROJECT

Z01-CL-08002-01 ANES

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

Application of somatosensory event related potentials to assessment of analgesia during general anesthesia.

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | |
|---|---|---|
| PI: | Michel Dubois, M.D. | ANES, CC |
| Other: | Monte Buchsbaum, M.D. | BPB, NIMH |
| | Richard Coppola, DSc | BPB, NIMH |
| | Prasad Gadde, M.D. | ANES, CC |
| | Alan R. Baker, M.D. | SURG, NCI |
| | Thomas Macnamara, M.B., Ch.B. | ANES, CC |

COOPERATING UNITS (if any)

CC, NIMH, NCI

LAB/BRANCH

SECTION

Anesthesia Section

INSTITUTE AND LOCATION

Clinical Center, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 3 | 3 | |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The primary goal of the protocol is to provide comparative data on the cardiovascular and central nervous systems, in order to assess analgesia during a general anesthetic. Continuous monitoring of heart rate, systolic, diastolic and mean blood pressure is done during the anesthesia, as indirect indices of autonomic nervous system activity. Periodic somatosensory evoked potentials after standard stimulation are collected, because they are preserved, even at deep levels of general anesthesia, and because certain components are modified by analgesics and by narcotic antagonists. Brain cortical activity is also assessed by EEG power spectral analysis. Data are colleced, processed and stored on-line by a mobile Digital Minc 11 computer. Changes, particularily in electrical reactivity of the brain are being compared, when different anesthetic techniques are used: when no narcotic is used, when small doses of narcotics are used and when large doses of narcotics are employed.

PHS-6040
(Rev. 10-76)

| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER |
|---|---|---|
|  |  | Z01-CL-08003-01 ANES |

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

Evaluation of Techniques for Peripheral Nerve Transection and Handling During Amputation and Their Relationship to Phantom Limb Phenomena.

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | |
|---|---|---|
| PI: | Yolanda Roth, M.D. | SURG, NCI |
| Other: | All Senior Staff | SURG, NCI |
| | Michel Dubois, M.D. | ANES, CC |
| | David Pickar, M.D. | BPB, NIMH |

COOPERATING UNITS (if any)

NCI, CC, NIMH

LAB/BRANCH

SECTION

Anesthesia Section

INSTITUTE AND LOCATION

Clinical Center, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 6 | 6 | |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Patients admitted to this protocol carry the diagnosis of osteosarcoma or soft tissue sarcoma, for which they receive one of the following amputations: forequarter, shoulder disarticulation, above elbow, below elbow, above knee or below knee amputation; also hemipelvectomy and hip disarticulation. This prospective study is designed to detect differences in the incidence of post amputation pain and sensation and neuroma formation as complications among patients who have their peripheral nerves transected at the time of amputation in one of three randomized way. Pain assessment is made throughout the study. Also venous serum endorphin levels are determined pre, peri and post operatively, and are being related to both the surgical stress and the anesthetic techniques. The anesthetic technique involves the use of mainly halogenated agents and excludes the use of narcotics.

PHS-6040
(Rev. 10-76)

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-08004-01 ANES |

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)
Effects of Narcotic and Brain Stimulation Analgesia on Human Chronic and Experimental Pain

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Richard Gracely, Ph.D. | Research Psychologist | NAB, NIDR |
| Other: | Ronald Dubner, DDS, Ph.D. | Chief | NAB, NIDR |
| | Raymond Dionne, DDS, Ph.D. | | NAB, NIDR |
| | Marvin Hoffert, MD | | NAB, NIDR |
| | David E. Lees, MD | Deputy Chief | Anesthesia Section |
| | Peggy Amato, RN | | NAB, NIDR |

COOPERATING UNITS (if any)
NAB, NIDR
Anesthesiology Section

LAB/BRANCH

SECTION
Anesthesiology Section

INSTITUTE AND LOCATION
Clinical Center, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 8 | 8 | |

CHECK APPROPRIATE BOX(ES)
☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The purposes of this study are threefold: (1) Assess the effectiveness of chronic electrical stimulation of midbrain sites for the relief of chronic pain in humans; (2) Evaluate the efficacy and mechanisms of traditional narcotic analgesia and compare these to that found for chronic electrical stimulation of midbrain sites; and (3) Validate experimental models of pain and their potential diagnostic use in chronic pain patients. In addition, this study will determine and compare the impact of both traditional narcotic and chronic electrical stimulation therapies on the functional, intellectual and emotional well being of these patients. Three types of participants in this study will be chronic pain patients who will receive surgically implanted stumulating electrodes for pain control, chronic pain patients maintained on traditional narcotic analgesics who will not receive implanted stumulating electrodes, and healthy normal volunteers. The effects of chronic brain stimulation in surgical patients will be compared to the effects of narcotics previously administered to these patients and to effects of narcotic regimes in nonsurgical chronic pain patients.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-08005-01 ANES |

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)
Pilot Study Examining The Effect of Whole Body Hyperthermia Combined With Adriamycin in Patients With Metastatic Sarcoma and Other Cancers

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Joan Bull, MD | Senior Investigator | COP, DCT, NCI |
| Other: | J. Whang-Peng, MD | Senior Investigator | COP, DCT, NCI |
| | William Schuette | Chief, ACE | BEIB, DRS |
| | David E. Lees, MD | Deputy Chief, Anes. | Anesthesiology Section |

COOPERATING UNITS (if any)

| | |
|---|---|
| NCI | Nursing, Clinical Center |
| Anesthesiology Section | BEIB, DRS |

LAB/BRANCH

SECTION
Anesthesiology Section

INSTITUTE AND LOCATION
Clinical Center, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 4 | 4 | |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Following phase I studies of whole body hyperthermia alone in the treatment of metastatic cancer, selected patients with sarcomas or other solid tumors were begun on a protocol combining adriamycin administered at 41.5 C with two hours of hyperthermia in excess of 41.5 C. Initial dosage was 10 mg/m$^2$ with escalation as subsequent patients entered the protocol.

The intercurrent administration of adriamycin (doxorubicin) and hyperthermia has not been fully evaluated yet for its tumoricidal potential, but there is evidence of acute synergistic toxicity in several patients. The combined use has been associated with conduction disturbances, arryhthmias and increased liberation of endogenous catecholamines. Clinical experience has shown conventional antiarrhythmia therapy to be effective. These results were first published by the Anesthesiology Section in JAMA 241:1816-1817, 1979.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-08006-01 ANES |

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)
Elucidation of basic mechanism of taste transduction by studying the effects of topically applied neuropharmocoligically active drugs on taste acuity in normal human beings.

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Carl Mattern, MD | Assistant Chief, LVD | NIAID, NIDR |
| Other: | Phillip Kapp, MD | Attending Anesthesiologist | Anesthesiology Section |

COOPERATING UNITS (if any)
NIAID, NIDR

LAB/BRANCH

SECTION
Anesthesiology Section

INSTITUTE AND LOCATION
Clinical Center, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2.0 | 2.0 | |

CHECK APPROPRIATE BOX(ES)
☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Stage I - testing the effect of an oral application of Succinylcholine on a volunteer to demonstrate the safety of the procedure and to determine the effect of taste. The starting dose was 2.5 mg in 5 ml water. It was increased to 20 mg in 5 ml water. There was no significant effect on taste sensation at these doses.

The project is now pending reassessment of protocol and approval to use larger doses of the test drug.

PHS-6040
(Rev. 10-76)

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|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-08007-01 ANES |

PERIOD COVERED
October 1, 1979 - March 30, 1980

TITLE OF PROJECT (80 characters or less)
Prevention of Post-Thoracotomy Pain by Bupivicaine (Marcaine) Nerve Block Anesthesia

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Eugene Woltering, MD | Clinical Associate | Surgery Branch, DCT, NCI |
| Other: | Phillip Kapp, MD | Attending Anesthesiologist | Anesthesiology Section |
| | M. Wayne Flye, MD | Senior Investigator | Surgery Branch DCT, NCI |

COOPERATING UNITS (if any)
NCI, CC

LAB/BRANCH

SECTION
Anesthesiology Section

INSTITUTE AND LOCATION
Clinical Center, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.5 | 1.5 | |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Post Thoracotomy pain patients were divided into three groups: one reviewed inter costal block with Marcaine in OR prior to closing the chest incision; one group had polyethylene catheters inserted in OR prior to chest closure for administration of Marcaine at six hour intervals postoperative; and the third group served as a control group receiving narcotic sedation as needed for postoperative pain. Narcotic sedation was also used in both Marcaine groups if needed for additional pain relief.

Preliminary results, still pending further analysis of data, seem to indicate:

1) There was no significant difference in the amount of MS used for postoperative pain relief in any group.
2) Although observers thought the Marcaine groups performed postoperative pulmonary function tests better than the control group, there was no statistical difference in any of the groups with regard to pulmonary function studies or arterial blood gases postoperatively.

PHS-6040
(Rev. 10-76)

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|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-08008-01 ANES |

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

A Phase I - II Trial of Hyperthermia and Methyl CCNU in Malignant Melonoma

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Joan Bull, MD | Senior Investigator | COP, DCT, NCI |
| Other: | J. Whang-Peng, MD | Senior Investigator | COP, DCT, NCI |
| | William Schuette | Chief, ACE | BEIB, DRS |
| | David E. Lees, MD | Deputy Chief, Anes. | Anesthesiology Section |

COOPERATING UNITS (if any)

| | |
|---|---|
| NCI | Nursing, Clinical Center |
| Anesthesiology Section | BEIB, DRS |

LAB/BRANCH

SECTION
Anesthesiology Section

INSTITUTE AND LOCATION
Clinical Center, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
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| 4 | 4 | |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The protocol has been modified such that methyl CCNU, an oral preparation, is no longer being used; BCNU, an intravenous agent, has been substituted. This was necessary since an efficacious drug level could not be demonstrated with the oral preparation and it was difficult to administer to a deeply sedated patient during hyperthermia. The intravenous preparation has shown a greater clinical response and permits a smoother treatment course.

PHS-6040
(Rev. 10-76)

October 1, 1979 through September 30, 1980

PUBLIC HEALTH SERVICE: NATIONAL INSTITUTES OF HEALTH

SUMMARY OF ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

BLOOD BANK DEPARTMENT:

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October 1, 1979, through September 30, 1980

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

# SUMMARY OF ANNUAL REPORT OF PROGRAM ACTIVITIES
# CLINICAL CENTER

## BLOOD BANK DEPARTMENT

### I. BLOOD BANK MISSIONS AND GOALS

The Blood Bank Department is a unique facility in a unique health care organization. The Department provides a full range of services commonly expected of blood banks at other institutions. In addition, we support a variety of research activities associated with the basic and clinical research missions of the National Institutes of Health.

Our primary mission remains the provision of an adequate supply of high-quality, safe blood and blood products to Clinical Center patients. It is upon this primary commitment to patients that the other goals and activities of the Blood Bank are based. In order to ensure that these service responsibilities are met in the most professional, timely, and economical manner, several service-related goals have been established for our Department.

The demand for specialized blood components for Clinical Center patients is increasing. Thus, one goal is to improve our technical expertise in component preparation by taking advantage of new advances. As improved components are requested for specific therapy, we plan to be at the forefront of developmental research. A second service goal is to increase our patient care consulting capacity in the expanding field of immunohematology and hemotherapy. We can contribute to optimal usage of available blood supplies. A third goal related to our service mission is to expand our blood donor base on the NIH campus, in NIH off-campus buildings, and among relatives and friends of Clinical Center patients. It is primarily through reliance on our fellow NIH employees that our blood and component supply needs are effectively and economically met. A further service goal is to expand our activities in testing, introducing, and incorporating new laboratory techniques and procedures related to blood banking. This improves the quality of the products and care we offer to Clinical Center patients.

A second mission of the Blood Bank Department is to maintain an active teaching program in immunohematology and blood transfusion. Formal training and education programs exist in the Department for medical technology students, for registered technologists who are specializing in blood banking, for medicine and pathology residents, and for physician fellows specializing in blood banking. We help train Clinical Center nurses who are learning the nursing skills related to blood transfusion. In addition, training experiences are often specially designed for visiting scientists and physicians. Our major goal related to our training mission is to update and improve our inservice teaching programs so that we continue to attract and train candi-

dates of the highest caliber. Training in the field of blood banking should bring Clinical Center Blood Bank programs to mind.

In addition to our inservice education programs the Blood Bank staff plays a substantial teaching role in the community. We assist with training programs for medical students, nurses, technologists and physicians in the area. Active faculty positions are maintained at Georgetown, George Washington, Johns Hopkins, and the Uniformed Services medical schools. Courses are taught to students in the FAES Graduate School at NIH. We participate in workshops and teaching programs in various parts of the USA. We strive to improve through education the level of blood bank practice in the Washington metropolitan area and throughout the country as well.

The emphasis placed on the research mission of the Clinical Center Blood Bank (CCBB) is one of the strengths of our organization. Our research programs have unquestionably strengthened the quality of our service and training programs. Contributions continue to be made in our traditionally strong research areas of viral hepatitis and immunohematology. In addition, research initiatives are being carried out successfully in innovative applications of cell separator technology, and, in the near future, HLA research and tissue typing. Our goals are to maximize the creative potential of our staff, to share our research findings with the rest of the professional community through publications and presentations, and to continually strive to secure new and constructive advances in our field.

The three missions of the Clinical Center Blood Bank - service, teaching, and research - are closely interrelated. Each of these areas is essential to the overall success of our organization. More specific objectives related to these goals will be found in Section IV.

## II. DEPARTMENTAL ACTIVITIES

### A. Service Responsibilities

More than 7,000 units of whole blood and red cells were transfused during the past year. Approximately 70% was drawn in our own blood bank, with the remainder supplied primarily by the Washington Regional Red Cross Blood Program. While still not self sufficient, provision of 70% of NIH's blood needs represents a further improvement from prior years (65% in 1979, 51% in 1978).

To improve blood collections we have utilized several approaches. The first has been to more actively collect blood outside of our facility. During the past year, we have conducted seven blood drives at NIH buildings off campus. Four of these were done jointly with the Washington Regional Red Cross. The other three were conducted solely by our staff. In addition, for the first time, three mobile drives on the NIH campus were conducted with the help of the Metropolitan Washington Blood Bank. This resulted in 125 additional units of blood for CC use which could be separated into components. Our second approach to improve blood collections has been to recruit donors from among the friends and relatives of patients. With the help of the Information Office, several approaches have been initiated; subsequently, we plan to assess their

effectiveness and see how to use this largely untapped source efficiently. Both programs should expand our ability to provide blood products to Clinical Center patients.

The Blood Bank increased production of fresh frozen plasma 20 percent, now approximately 120 units per month. We produced more than Clinical Center patients used for the second consecutive year. The balance was exchanged with local hospitals for other components needed by Clinical Center patients; this helped the general, regional supply of plasma. Sufficient cryoprecipitate was prepared to meet the supplemental needs of Clinical Center patients. As they were, last year, the out-patient hemophilic patients were treated primarily with Factor VIII commercial concentrate acquired both by direct purchase and by exchange for outdated plasma.

Blood Bank physicians continued to perform clinical consultations on patients with immunohematological problems and suspected viral hepatitis after transfusions. For example, more than 80 reported transfusion reactions were evaluated, two thirds of these were in fact transfusion related. Blood Bank consultants were active in evaluating intraoperative coagulation problems. They are currently involved in techniques for intraoperative blood salvage to decrease the use of blood products during surgery.

The Blood Bank assumed a more active role in therapeutic procedures during the past year. Numerous manual phlebotomies were performed on patients with polycythemia and hemochromatosis. The addition of a third cell separator, a Haemonetics model 50, enabled us to perform approximately 25 therapeutic procedures per month. Besides removing blood constituents, we did plasma exchanges in patients with systemic lupus erythematosis, Waldenstrom's macroglobulinemia, hyperlipoproteinemia, aplastic anemia, and a variety of neurological conditions. Additional automated red cell exchanges in polycythemic patients were completed, giving us the largest reported experience with this procedure in the world. Approximately 50 cell separation procedures are now performed each month, a doubling of last year's procedures. We are now recognized nationally as a leading center in therapeutic apheresis application and research.

The Plateletpheresis Center, in its seventh year on an NCI contract, continued to function at close to maximum capacity. The Center recruited more than 3500 donors and performed more than 3300 four-unit manual plateletphereses. The Blood Bank monitored its performance. In addition, we produced 15% of the platelets used by Clinical Center patients using single donor units and automated pheresis, an increase of 5% over the previous year.

The Blood Bank continued to meet an increasing number of requests for blood products from the NIH research community. We performed more than 20 manual plasmapheresis and 20 automated pheresis procedures per month for research. Approximately 350 blood samples per month were drawn in the Blood Bank for NIH laboratory studies. Often, specialized methods of collection and preservation were required for such products as granulocytes, lymphocytes,and monocytes. We have supplied plasma for experimental blood products, e.g., for the clinical use of an $\alpha$-1 antitrypsin concentrate. Such products often cannot be obtained elsewhere in the quantity and quality necessary for NIH researchers.

The Blood Bank immunohematology reference lab continued to investigate difficult serologic problems referred by physicians in area hospitals and throughout the country. Approximately 90 such problems were investigated over the past year. In one instance, this laboratory provided the answer for a fatal transfusion reaction at a local hospital. The elucidation of these cases has not only served the referring facility but has provided excellent source material for teaching and for additional investigation. The Blood Bank has received commendations from several community hospitals for the reference role it plays.

## Department Organization

The Blood Bank Department's Organizational Chart is on page BB-15. The Blood Services Section was split into a Laboratory Section and a Phlebotomy-Pheresis Section. Separating the functions of these two Sections will enhance the service, supervision, and research activities of each. Dr. Richard Davey became head of the Laboratory Section and Dr. Harvey Klein remained head of the Phlebotomy-Pheresis Section.

Ms. Shirley Sakas was appointed Technical Supervisor of the Laboratory Area upon the transfer of Ms. Mary Gustafson to the FDA. Ms. Elsie Yanchulis was appointed Supervisory Clinical Nurse upon the retirement of Ms. Wanda Chappell. Wanda Chappell was the first nurse hired in the Blood Bank 27 years ago and had been the Chief Nurse for all of that time.

## C. Donor Program

The Blood Bank continued its policy of using all volunteer blood. Current active donor rolls stand at 2297. We have extensive information on each donor related to red cell suitability which is computerized for rapid recall for phlebotomy and transfusion. On campus, the Blood Bank continued recruitment drives and began to more actively seek blood donations from the relatives and friends of patients. The Blood Bank has continued its own successful mobile blood drives at the NIH Poolesville campus and at the Federal and Blair buildings, expanded its joint drives with the Washington Regional Red Cross at larger off-campus buildings, and initiated joint blood drives with the Metropolitan Washington Blood Banks at buildings on the NIH campus. Approximately 250 NIH employees attended our first Donor Appreciation Party on 8/13/80. Donor prizes were provided by the Recreation and Welfare Association, "Stop Give Blood" T-shirts were given to the first 200 donors by the CC Information Office, and refreshments were served by the Blood Bank Staff. By these various mechanisms we have expanded our ability to draw blood for our own use and increased the number of units collected in our region without an increment in personnel or expenses.

Despite the continued rift between the major national blood suppliers, the NIH Blood Assurance Program continued to run smoothly. Relatives of NIH employees received more than 350 credits or actual units of blood across the country. In one instance, eighty units were supplied to Charity Hospital in New Orleans for the relative of an NIH employee.

## D. Laboratory Service

The Blood Bank Laboratory, divided into Compatibility Testing and Donor Processing areas, continued to provide comprehensive service utilizing extended hours of operation and an "on call" system. During the past year the laboratory staff determined the blood group and type of 3090 patients, performed 3480 direct Coombs tests, 5150 patient screening tests for irregular antibodies, and 10,200 crossmatches. The "routine" laboratory work once again succeeded in the solution of far from "routine" problems. The staff identified five or more antibodies in the serum of several patients. The laboratory assumed the further role of conducting $^{51}$Cr red cell survival studies as an "in vivo" crossmatch technique for numerous problem patients.

All blood products collected at NIH for patient use are processed and issued by the Blood Bank. For example, the laboratory continued its responsibility for processing and issuing granulocyte concentrates collected by NCI. Blood products for immunocompromised patients were irradiated in the CCBB to obviate graft versus host disease.

## E. Professional Activities

The professional staff has continued to participate actively in a wide variety of local, national and international meetings and programs during the past year.

Dr. Paul V. Holland continued to serve on the Technical Manual Committee of the American Association of Blood Banks, on the American Red Cross Research Review Committee, and as Chairman of the NHLBI Policy Board for the Transfusion Transmitted Viruses Study. He became a member of the Safety and Efficacy committee for the NIAID sponsored hepatitis B vaccine study in patients and staff of renal dialysis units. He lectured frequently at area facilities such as Howard University, Walter Reed Hospital, and the Institute of Chemists. He directed the FAES course Immunology 508M and spoke at regional blood banking meetings in Kentucky, Illinois, and Washington, D.C., as well as the International Society of Blood Transfusion meeting in Montreal, Canada.

Dr. Harvey J. Alter was an invited speaker at several major symposia and scientific meetings. These included an International Symposium on Virus and the Liver in Basel, Switzerland; an International Kidney Conference in Reston, Virginia; a Canadian Liver Foundation meeting on pediatric liver disease; the International Society of Hematology meeting in Montreal, Canada; an Aspen, Colorado Conference on Safety in Transfusion Practices and a joint U.S.-Japanese Symposium in New York. In addition, he spoke at Johns Hopkins and other area hospitals and lectured in two FAES courses. Dr. Alter continues to serve on the Medical Advisory Committee of the Washington Red Cross, on the Scientific Program Committee of the American Association of Blood Banks, and the Clinical Research Subpanel of NIAID. In addition, this year Dr. Alter served on the Advisory Committee to the Hepatitis B Vaccine Efficacy Trials and served as Chairman of their only subcommittee. Dr. Alter was also cochairman and organizer of a workshop on serologic tests for non-A, non-B hepa-

titis in Vienna, Austria and was selected as co-chairman of the Organizing Committee for a 1981 International Symposium on Viral Hepatitis. Dr. Alter will serve as one of the editors of the Viral Hepatitis Symposium proceedings and was also selected as guest editor for the first issue of a new journal, "Seminars in Liver Disease."

Dr. Harvey G. Klein continued as consultant to the Johns Hopkins Hospital Hematology Clinic and was a speaker at hematology and clinical pathology grand rounds there. He served as chairman of the Regionalization Committee of the Metropolitan Washington Blood Bank Association and as Secretary of that organization. He participated in a National Science Foundation supported study of phlebotomy in chronic high altitude sickness which was conducted in the Peruvian Andes. He was invited to speak at the Red Cross Apheresis Symposium in Chicago, at the Emory University Apheresis Symposium in Atlanta, at Georgetown University, and at Howard University's Symposium on Sickle Cell Disease. He continued as attending physician for Clinical Hematology (NHLBI) and remained on the faculty of the Uniformed Services University of Health Sciences, the FAES course Immunology 508, and the Nursing Department's blood transfusion course.

Dr. Richard J. Davey is clinical assistant professor of medicine at Georgetown University Hospital; he served as attending physician for the Department of Medicine, as instructor for the second year medical school course in hematology, and as a speaker at the Georgetown hematology conference. He spoke at the Department of Pathology rounds at Providence Hospital, at the University of Virginia and at the University of California, San Francisco. He was a member of the NIH Clinical Center Education Coordinating Committee and coordinator of educational activities in the CCBB. He was a faculty participant in the USUHS pathology course and the FAES sponsored Immunology 508. For the Nursing Department's blood transfusion courses which trained 217 CC nurses this past year, he was the coordinator for the Blood Bank teaching effort and one of the lecturers.

Ms. Mary H. McGinniss continued to serve on the Standards Committee for the American Association of Blood Banks. Ms. McGinniss conducted numerous teaching sessions in immunohematology throughout the year, was a guest lecturer in Immunology 508M, and participated in the Clinical Pathology Department conferences. Ms. McGinniss was an invited guest speaker at the Virginia Society for Medical Technology meeting and the American Red Cross Reference Laboratory Conference, both in Virginia.

Ms. Shirley Sakas, now Technical Supervisor, is also serving as Acting Education Coordinator for the Specialist in Blood Banking (SBB) students. She attended several management and supervisory courses sponsored by NIH.

The Blood Bank was the co-sponsor of the First International Autotransfusion Symposium held in Baltimore, Maryland, April 24-25, 1980.

## Honors and Awards

Ms. Darlene Kent received a Quality Increase for her outstanding work performance.

Ms. Frances Chichester received a Cash Award for her outstanding performance as a Stay-In-School employee.

Ms. Sandra Rosen and Ms. Virginia Weber received Cash Awards for their outstanding work performance in the Department's newly established Pheresis Unit.

Mr. Victor Chance received a Cash Award for his continuous outstanding work.

Ms. Elsie Yanchulis received a Cash Award for her recommendation involving the safe storage of emergency platelets.

Dr. Harvey G. Klein received the PHS Commendation Medal for establishing a model Pheresis Unit at the Clinical Center which engaged in novel therapeutic approaches for a wide variety of diseases.

The Blood Bank Department was voted first among Clinical Center services in a poll of Clinical Associates. This is the third year in a row the Department has been so honored. The Clinical Pathology residents also ranked the Blood Bank Department number one among all the services they had rotated through.

## III. MAJOR PROGRESS

### A. Hepatitis

#### 1. Post-Transfusion Hepatitis (PTH)

An ongoing, controlled, prospective study continues to yield valuable insights into the nature of PTH. In this study, multiply transfused open heart surgery patients are carefully followed for nine months after surgery, as is a control group consisting of non-transfused patients undergoing cardiac catheterization. While the main thrust of this study has been to define the frequency and etiology of PTH, other aspects of the study are now assuming increasing importance. It was an earlier phase of this study which first demonstrated the existence of non-A, non-B (NANB) hepatitis. This entity now constitutes greater than 95% of our PTH cases. As these cases continue to occur, we are accumulating a large number of patients (60 at present) who are serving to define the clinical spectrum and chronic sequelae of NANB hepatitis. It has become evident that this is generally a mild disease in its acute stage; but, with frequent progression to chronic liver disease, NANB may be the most consequential of all forms of PTH (see below). In addition to defining the clinical spectrum of NANB hepatitis, the study is providing an invaluable resource of pedigreed donor and recipient serums for use in the development of serologic tests and for the investigation of transmission patterns in chimpanzees.

At the time of last year's annual report, we were in the process of summarizing the overall data from this study with the intent of publication. However, the literature indicated that a test for NANB carrier donors might be imminent so we elected to continue the study until such a test could be implemented. As it turned out, a confirmed test for NANB has not been established, and the immediate prospects for such a test are not favorable (see

below). In the interim, however, we have established that bloods from donors with an elevated transaminase (ALT) result in significantly more recipient hepatitis than bloods from donors with a normal ALT (see below). We therefore plan to implement ALT screening of NIH blood donors and to exclude blood from donors whose values are elevated. It is anticipated that this measure will reduce the incidence of PTH by approximately 45%. The frequency of PTH after routine ALT testing will be compared a) with that obtained in our current study, b) with that in patients receiving Red Cross blood (which currently cannot be prospectively screened for ALT), and c) with that in our non-transfused controls. The initiation of this study, involving an ALT presreened donor population, will also serve as the end-point for our current study. If and when a practical test for NANB is developed, then such screening will be combined with ALT testing and incorporated into the same study.

2. Relation of Donor Transaminase (ALT) to Recipient Hepatitis

During the course of the current prospective PTH study, encompassing approximately 650 patients and 200 controls, we began testing donors for ALT. Because these tests were performed off-campus, ALT results were not known until after transfusion. We have now followed 237 patients in which all donor serums were tested for ALT. Of 182 patients receiving blood in which all donor ALT's were less than the upper limit of normal (45 IU/L), 20 (11%) developed hepatitis. Of 55 patients who received at least one unit of blood with an ALT value greater than 45 IU/L, 15 (27%) developed hepatitis. The risk of developing hepatitis was thus significantly greater ($p < .01$) if blood with an elevated ALT was transfused. However, 57% of patients who developed hepatitis received only blood with a normal ALT level. Overall, 2.4% of the donor population had an elevated ALT. This study would then predict that exclusion of donors with an elevated ALT might prevent approximately 45% of PTH but would necessitate the loss of only 2.4% of the donor population. We feel that these data, along with those of a study sponsored by the NHLBI, warrant the interdiction of blood donors with an elevated ALT. We are in a position to evaluate the effect of ALT screening in a prospective fashion; the majority of our blood is from NIH donors and can be tested for ALT prior to transfusion, whereas some is from the Red Cross where ALT testing will not be done. Thus, we plan to initiate ALT screening as soon as a protocol can be developed and a mechanism for rapid ALT screening established.

3. Chronic Hepatitis

One of the most striking findings to evolve from the transfusion studies is the frequency with which NANB hepatitis progresses to chronic liver disease. We continue to find that approximately 50% of patients with NANB hepatitis have abnormal ALT's for at least one year after the onset of disease. In addition, there are other patients who apparently recover only to demonstrate a recurrence of elevated ALT levels 6 months to one year later. It cannot yet be proved, but it is almost certain that there are additional patients who normalize their ALT, but nonetheless become chronic carriers of the NANB virus. Thus, perhaps as many as 75% of patients with NANB hepatitis proceed

to develop some chronic manifestation of this disease; we have biopsy data on 16: 10 (62%) have chronic active hepatitis, 4 (25%) have chronic persistent hepatitis and 2 (13%) have cirrhosis. We have had occasion to rebiopsy three patients whose initial biopsy showed chronic active hepatitis; all three showed decreased inflammation in the second biopsy without progression to cirrhosis. However, another patient died with severe cirrhosis, 10 years after an acute episode of NANB PTH.

Thus, although it appears definite that some NANB cases evolve into cirrhosis, the majority of cases seem to have a very slowly resolving disease as evidenced by gradually decreasing ALT levels and by improved liver biopsy morphology. We will continue the long term follow-up of patients with chronic NANB hepatitis in conjunction with the NIAMDD Liver Service in the hopes of better defining what is perhaps the major non-alcoholic cause of chronic liver disease in the U.S. Peripheral to these investigations is a study with Drs. Dean Mann and Jay Hoofnagle to determine if there are any HLA patterns which distinguish patients who develop chronic NANB hepatitis from those who completely recover from their acute episode.

We are also doing thin section electron microscope studies on liver biopsy specimens. This year, for the first time, we detected intranuclear particulate structures in three patients similar to those previously observed in the chimp model (see below). The significance of these ultrastructural changes is still unclear.

### 4. Chimpanzee Studies

We are now near completion of a series of three sequential homologous challenge and cross-challenge studies of NANB hepatitis. These studies, performed in six chimpanzees, attempted to document the existence of more than one NANB agent by inducing a second distinct episode of NANB infection. To date, these studies have not provided evidence for multiple NANB agents; similar studies from two other labs imply that there are at least two NANB agents.

The most interesting aspect of these challenge studies has been the definite development of chronic hepatitis in three of the six chimps infected and the possible development of chronic hepatitis in a fourth chimp. One chimp in another study has also developed chronic hepatitis. Thus the inordinately high incidence of human NANB chronic liver disease is confirmed in the chimpanzee model. These animals might now serve to test the efficacy of anti-viral agents such as adenine arabinoside and interferon to abrogate the chronic hepatitis and/or infectivity of these animals. Such studies would parallel those now being done in humans for hepatitis B.

In a collaborative study with LID/NIAID last year we reported that two distinct ultrastructural changes were seen in acute phase liver biopsies of chimps infected with NANB. Some chimps developed cytoplasmic changes and others nuclear changes but the two were mutually exclusive. This suggested two etiologic agents. Unfortunately, in the past year we have found some inocula which transmit both types of changes and some chimps who initially have the cytoplasmic change transmit the nuclear change. These ultrastructural changes may thus represent different stages of the same infection

rather than two distinct infections. Studies are in progress to try to sort this out.

Our studies of the efficacy of frozen red cells (FRBC) in the prevention of NANB hepatitis have been in limbo because of the transfer of 10 NHLBI-owned chimps from New York to San Antonio. These studies are now to be resumed. We have collected units of frozen blood from four donors with persistently abnormal ALT levels; each donor has been implicated in at least one case of PTH. These FRBC units will be transfused to chimps; inoculation of the plasma removed at the time of freezing will serve as the control if no hepatitis develops. If FRBC are not infectious, but the homologous plasma is, then the efficacy of freezing blood will have been supported. Conversely, if the FRBC infect chimpanzees, then the efficacy of FRBC for hepatitis prevention will have been disproved for NANB (as well as for type B disease as we demonstrated previously).

This year, using inocula from our heart study patients, Dr. Feinstone of NIAID transmitted NANB to the marmoset, thus providing a second animal model for this disease. With Dr. Feinstone, we have also expanded our serial passage studies (six serial passages now documented in chimps) and have titered some of our inocula; one acute phase NANB inoculum is still infectious when diluted $10^6$ and possibly when diluted $10^8$.

5. NANB Serologic Methods

A major effort has been expended in the past year to establish a serologic test for NANB. This was spurred not only by the importance of such a test, but by three published reports suggesting that simple methods could detect NANB antigens and antibodies. Despite the use of multiple, very well characterized acute and convalescent human and chimpanzee serums, we were unable to confirm published work. Precipitin lines were indeed observed, but they appeared to be non-specific and/or artifactual. Because other laboratories also had difficulty in confirming these tests, a NANB workshop was convened in Vienna, Austria in June of this year. Dr. Alter served as co-chairman of the section on serologic diagnosis; prior to the meeting he was responsible for the organization and distribution of a coded panel consisting of serums proven to transmit NANB to chimpanzees, serums claimed to contain a NANB antigen and a negative control serum. The panel also included "antibodies" utilized in several laboratories to detect "NANB antigens." This panel was distributed to the 13 laboratories most actively engaged in serologic tests for NANB. The code was broken at the meeting; it revealed wide discrepancies from laboratory to laboratory and some discrepancies within a laboratory, as indicated by variant results on duplicate analysis.

The laboratories which detected the most positives also found the negative control to be positive. Overall, it was felt that there is a high degree of non-specificity in immunologic test systems for NANB. Whether or not there was a specific precipitin system masked by non-specificity could not determined by this panel. It was felt that a larger panel with more be negative controls and more type A, type B and toxic hepatitis controls was required; Dr. Alter will try to assemble and distribute such a panel in

the next several months. At the same time, the CCBB will continue a search for better NANB reagents. We are also continuing to pursue the possibiity of disassociating NANB antigens and antibodies from immune complexes isolated by the RAJI cell technique. This latter study is being conducted with Dr. Jules Dienstag in Boston.

### 6. Vaccine Studies

Two major hepatitis B vaccine studies are being conducted in the U.S. Both emanate from the New York Blood Center; one, in male homosexuals, is funded by Merck Institute and the other, in renal dialysis patients and staff, is funded by NIAID. Dr. Alter is on the advisory committee of the homosexual study and is a co-participant in the dialysis study. Dr. Holland is on the Safety and Data Monitoring Committee of the dialysis study. The homosexual trial is now almost complete, so the code will soon be broken and the results analyzed. Accession into the dialysis study has been taking place over the past year; it has entailed considerable effort due to initial resistance by both patients and staff. Accession is now, however, proceeding very well; it is hoped that this study will be completed over the next year. No major safety problems have been encountered, but no statement regarding efficacy can be made because of the double blind conduct of the study.

### B. Immunohematology

Two major research projects continue in the Immunohematology Laboratory. One concerns the effect of bacterial or viral infections on red cell antigens and on the stimulation of unexpected allo- and auto-antibodies. To date, selected bacteria appear to have Kell-like interior antigens and $Jk^b$-like exterior antigens. Case studies have demonstrated that some septic patients can both acquire a non-genetic Kell-like antigen on their red cells and produce an IgM, saline reacting anti-Kell. Other studies have correlated auto-anti-$Jk^b$ antibodies and subsequent clinical hemolysis with certain bacterial infections. New findings this year include a possible correlation between certain herpes virus infections and the production of a rare auto antibody, anti-$Pr_a$, and the identification of several bacteria which can convert Le(a-b-) cells to Le (a+b-) cells. The latter may be a partial answer to the prevalance of IgM anti-$Le^a$ antibody.

The second major project concerns continuing work on the malaria receptor antigens for both _P. vivax_ and _P. falciparum_. It has been proved both _in vitro_ and _in vivo_ that the presence of the Duffy ($Fy^a$ and/or $Fy^b$) antigens is the key to the erythrocyte incorporation phase of the _P. vivax_ life cycle. In 1979, it was found that Duffy antigens could be separated from the red cell membrane in a soluble form. Once these soluble antigens can be stabilized, then work will proceed in characterizing the exact biochemical nature of the malaria receptor. Subsequently, attempts will be made to block red cell invasion by merozoites with the soluble product. _P. falciparum_ red cell receptors have been more difficult to elucidate, but work with rare red cells has suggested that the invasion receptor is involved with glycophorin-A. Therefore, new work involves separating glycophorin-A into its component

parts and testing any rare red cells lacking glycophorin-A, such as En(a-) cells and cells lacking M and N antigens, in invasion studies.

## C. Clinical Immunohematology and Tissue Typing

The Blood Bank professional and technical staff is pursuing a variety of clinical projects in the fields of hematology, immunohematology, and tissue typing. For example, additional $^{51}$chromium red cell survival studies have been performed on patients with anti-Le$^b$ antibody; a clear relationship between in vitro thermal activity of the antibody and in vivo red cell survival has been established. A patient with an antibody against the high frequency Yt$^a$ antigen was studied and the characteristics of this unusual antibody clarified. The cumulative experience with $^{51}$Cr rbc survival studies has led to the recommendation that the 24 hour rather than the 60 minute survival value be the primary determinant of transfusion safety. The association between anti-c and and anti-E antibodies and the potential risk of transfusing blood from a donor with anti-penicillin antibody to a patient on penicillin or a related drug continue to be investigated.

New studies include an evaluation of the post-transfusion survival of maximally stored, deliberately "undercollected" units of red cells. If these cells survive adequately when chromium labeled and reinfused, a recommendation can be made to modify the volume of blood which may be drawn from a donor, thus salvaging units which are now discarded. Another new study is designed to evaluate, by means of $^{51}$Cr survival studies, the in vivo significance of red cell allo-antibodies reactive only with enzyme treated red cells.

A new method of storing platelets called "temperature-cycling" will be studied under a joint protocol with the American Red Cross. If this clinical study supports in vitro work already completed, an extension of the present 72 hour storage limit for platelets can be recommended.

The Blood Bank Department's HLA Typing Laboratory is now operational. It is rapidly becoming involved in a variety of research and service related projects. In-house projects are underway investigating 1) the pattern of HLA antibody formation in multi-transfused cardiac patients, 2) the presence of HLA antigens on young red cells (neocytes), and 3) the HLA antigen distribution of high altitude Peruvian Indians. Collaborative HLA projects have been initiated with investigators of the NHLBI and NIAID, as well as with research groups at the American Red Cross and Georgetown University Hospital.

## D. Pheresis and Component Therapy

The Blood Bank has expanded its research studies using cell separator technology. In collaboration with Clinical Pathology's Hematology Section, NHLBI and NCI, the production of young red cells or "neocytes" was first demonstrated to be feasible. $^{51}$Cr survival studies in three volunteers and seven thalassemic patients showed then that this product has a survival superior to that of standard fresh or frozen red cells. Now clinical trials with three thalassemic patients, at NIH and at Columbia University, are in progress. While these studies are being carried out, a new method of neocyte collection,

using a commercially available cell washer, is being investigated. This could make neocyte collection easier and more practical.

Collaborative studies with Walter Reed Army Institute of Research, NHLBI and CDC have focused on the role of phlebotomy in various polycythemic states and the physiologic consequences relating to exercise and oxygen delivery. Patients with such diverse conditions as high $O_2$-affinity hemoglobinopathy, familial erythrocytosis, and high altitude polycythemia have been studied using an automated red cell exchange protocol. With the support of the National Science Foundation, these studies have been further pursued in the Peruvian Andes at the world's highest permanent laboratory; these are the first such studies ever performed and the first time a cell separator has been used at this altitude. The results should have a major impact upon the concept of chronic, high altitude sickness and its management.

Controlled studies of plasma exchange and lymphocyte depletion continue to expand. These now encompass Grave's disease and systemic lupus erythematosis (inconclusive thus far), aplastic anemia and pure red cell aplasia (extremely encouraging), and schizophrenia (disappointing to date). Studies of patients with a variety of neurologic conditions and of the kinetics of ceramide trihexoside in Fabry's disease have been performed on the cell separator. Finally, preliminary studies are underway to characterize optimum conditions for collecting circulating stem cells from the peripheral blood using the cell separator. Collaborative research projects in the apheresis area have been restricted only by the limitations of machine availability and personnel time.

## IV. FUTURE OBJECTIVES

The Blood Bank Department continues to focus on its primary responsibilities of service, teaching, and research in planning its future goals and objectives. The past year has been one of growth and accomplishments. We plan to build on this record in determining and obtaining our objectives for the future.

### A. Service:

Increasing reliance on NIH blood donors will be achieved through continued expansion of "mobile" blood drives to satellite NIH buildings. Some of these drives will be with the Red Cross and others will be with the Metropolitan Washington Blood Bank. Automated pheresis machines will be used more extensively for obtaining key blood components such as plasma and platelets. The recent acquisition of a Haemonetics Model 50 pheresis machine will allow us to achieve component preparation goals safely and efficiently. If space and staffing requirements are fulfilled, the newly developed HLA lab will be able to provide in-house tissue typing services to NIH investigators. The plan for assumption by the CCBB of the NCI contract for plateletpheresis would centralize management of the collection, processing, and distribution of blood and most blood products at the Clinical Center. Actual incorporation of the plateletpheresis operation would result in more efficient and more economical platelet concentrates for CC patients.

B. Teaching:

The Blood Bank was once again ranked first as a training and service facility by both clinical pathology residents and clinical associates. Revisions and updating of the physician's training curriculum, however, will continue. A new videotaped lecture series on principles of blood transfusion will be completed for use by the Clinical Center nursing staff. The existing curriculum for SBB training, and the FAES Immunology 508 course schedule will be reviewed and upgraded as necessary. Formal teaching affiliations will be established with the hematology divisions at Georgetown and George Washington University Hospitals for CCBB training of hematology fellows as the Clinical Pathology residency program is phased out at the Clinical Center.

C. Research:

Research goals and objectives for the Blood Bank Department will be focused in the areas of hepatitis, therapeutic pheresis, immunohematology, component therapy, and HLA typing. Attempts will continue to identify a serologic marker for non-A, non-B hepatitis and to further characterize post-transfusion hepatitis in the multi-transfused patient. An investigation of the use of serum enzymes as nonspecific identifiers of hepatitis carriers in blood donors will be initiated. Research protocols involving red cell or plasma exchange in diseases such as aplastic anemia, amyloidosis and schizophrenia will continue; it is anticipated that additional protocols will be initiated as staffing and space allow. Studies on young red cells ("neocytes") will also continue, and further data accumulated as to their use in the clinical support of the chronically transfused patient. Within the next year we hope to have an easy, more practical method to provide this blood product. Increased research involvement by the main Blood Bank laboratory will be encouraged, with further in vitro and in vivo study of poorly characterized red cell allo-antibodies planned. Immunohematology research will include investigation of red cell antigen and antibody changes associated with certain malignant and infectious diseases. New protocols designed to examine specific storage requirements for red cells and platelets will be initiated. The HLA laboratory will be increasingly involved in a variety of studies involving population genetics, disease association, and characteristics of HLA antibody formation.

The Blood Bank staff looks forward to the successful attainment of these service, teaching, and research objectives. They all pertain to our overiding goal of providing the best care for our patients.

## V. Blood Bank Department Organizational Chart

### LABORATORY SERVICES SECTION

Anderson
Casper
Coles
Craven
Dorset
Eberhard
Ellis
Gregg
Marotto
Mucciariello
Mueller
Tysdal

Sakas
(Supervisor)

CHIEF: DAVEY

### BLOOD SERVICES SECTION

Phlebotomy

Chance
Davis
Kirkwood
Sanborn

Cahill
Mason
Meyer
Morgan
Moroney
Nilsen
Wells

Pheresis

Cunningham
Everett
Jack
Quail
Rosen
Weber

Yanchulis
(Supervisor)

CHIEF: KLEIN

### IMMUNOLOGY SECTION

Hepatitis

Hudson
Rountree
Shoup

Koziol
(Supervisor)

Solomon

Immunohematology

McGinniss

CHIEF: ALTER

### OFFICE OF THE CHIEF

Chichester
Kilmain
Orr
Shawver

Lenes
Bracy
Simon

Recruiting Unit

Brown
Driscoll
Kabel
Kendall

Colbert
(Supervisor)

ASST CHIEF: KLEIN
CHIEF: HOLLAND

## VI. PUBLICATIONS

1. Berman, M.D., Alter, H.J., Ishak, K.G., Purcell, R.H., and Jones, E.A.: The chronic sequelae of non-A, non-B hepatitis. Annals of Internal Medicine. 91: 1-6, 1979.

2. Dienstag, J.L., Bhan, A.K., Alter, H.J., Feinstone, S.M. and Purcell, R.H.: Circulating immune complexes in non-A, non-B hepatitis. Lancet I: 1265-1267, 1979.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02001-05 BB |

PERIOD COVERED

October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

$^{51}$Cr RBC Survival as a Means of Defining the in vivo Characteristics of Red Cell Alloantibodies

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Richard J. Davey, M.D., Chief, Laboratory Section, Blood Bank Department, CC

Others: Paul V. Holland, M.D., Chief, Blood Bank Department, CC
Harvey J. Alter, M.D., Chief, Immunology Section, CCBBD
Sandra L. Rosen, M.T. (ASCP), Blood Bank Department, CC

COOPERATING UNITS (if any)

LAB/BRANCH

Blood Bank Department

SECTION

Immunology Section

INSTITUTE AND LOCATION

Clinical Center, Building 10A, Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
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CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

In the first phase of this project the rapid sequence $^{51}$chromium red cell survival test proved to be a valuable test in the evaluation of the clinical significance of irregular red cell antibodies. It is now a widely accepted laboratory procedure used primarily in situations when compatible blood cannot be found by usual in vitro serologic techniques.

The project, therefore, now concentrates on those patients and blood donors who have poorly understood and incompletely characterized red cell antibodies detected in their serum. Characterization of the in vivo significance of these antibodies will allow more rational selection of blood for these people should transfusion be necessary in the future.

A study of the significance of anti-H in the rare "Bombay" patient, and two papers describing unusual serologic problems solved by the $^{51}$Cr technique have been published. Studies continue investigating the significance of the Lewis$^{b}$ antibody and, in collaboration with the Red Cross, the clinical significance of certain variations observed in the direct antiglobulin test.

Z01-CL-02001-05 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 - September 30, 1980

Project Title: A Rapid Technique for Determining In-Vivo Red Cell Survival in Patients Demonstrating In-Vitro Incompatibility with all Donor Red Cells

Previous Serial Number: Z01-CL-02001-04 BB

Principal Investigator: Richard J. Davey, M.D.

Other: Paul V. Holland, M.D.
Harvey J. Alter, M.D.
Sandra L. Rosen, M.T. (ASCP)

Cooperating Units: None

Man Years: Total: 1
Professional: 1

## Project Description

### Objective:

1. To utilize a rapid $^{51}Cr$ survival procedure to clarify the clinical significance of certain poorly understood or incompletely characterized red cell antibodies (e.g. anti-H in Bombay O, anti-Chido).

### Methods Employed:

A small sample (1.0 - 2.0 ml) of test red cell suspension is labeled with 20 u Ci of $^{51}Cr$, washed, and infused into the patient. Serial blood samples are subsequently drawn and the survival characteristics of the infused cells determined by measuring the radioactivity of each sample.

### Major Findings:

Since approval of this study the following observations have been made.

A. A case of "saline agglutinating phenomenon" has been documented and described. Patients with this phenomenon have a serum factor which agglutinates all red cells which have been washed in saline, thus complicating laboratory crossmatching efforts and rendering the infusion of saline containing fluids potentially hazardous. Survival studies using cells

washed in various media permitted a decision to be made which resulted in a safe open-heart surgical procedure being done on this patient.

B. People with the rare inherited blood group called "Bombay O" have in their serum an antibody which reacts in vivo against all normal ABO blood groups. The clinical significance of this antibody was investigated through $^{51}Cr$ survival studies in a person with the "Bombay O" blood group. It was determined that the antibody was strongly active in vivo and that "Bombay O" people can safely receive blood only from other "Bombay O" donors.

C. Patients who required transfusion with panagglutinating antibodies and antibodies against high incidence or poorly described RBC antigens were studied. The clinical significance of each patient's antibodies was determined by a $^{51}Cr$ survival study, with decisions made as to the relative safety of transfusion.

D. A series of patients with the commonly encountered alloantibody, anti-Lewis$^b$, are being studied. The in vivo potency of this antibody has never been clearly defined. Our findings show that the in vitro thermal reactivity of the antibody correlates closely with in vivo red cell survival.

E. Two patients without serologic evidence of incompatibility were found to have shortened $^{51}Cr$ RBC survival when red cells of selected phenotype were transfused.

F. Based on 37 $^{51}Cr$ red cell survival studies, we have recommended that the 24-hour survival value be used as the primary determinate of transfusion compatibility, rather than the currently used 60-minute value.

Significance to Biomedical Research and the Program of the Institute:

The primary goal of the Clinical Center Blood Bank is to provide safe blood products to Clinical Center patients. This $^{51}Cr$ red cell survival procedure has proven to be a valuable tool in defining the relative safety of transfusion in patients for whom compatible blood cannot be found by in vitro techniques. If this procedure continues to prove its significant clinical value, it is hoped that it will become a widely used blood bank service. In addition, use of this technique will provide greater understanding of the clinical importance of certain red cell antibodies which are now incompletely characterized.

Proposed Course:

Continued use of $^{51}Cr$ survival technique in appropriate patients.

Publications:

1. Davey, R., Tourault, M., and Holland, P.: Significance of Anti-H in the Bombay ($O_h$) Patient, Transfusion 18: 738, 1978.

2. Davey, R., Gustafson, M., and Holland, P.: Accelerated Immune Red Cell Destruction in the Absence of Serologically Detectable Alloantibodies, *Transfusion* 20: 348-353, May-June, 1980.

3. Davey, R., O'Gara, C., and McGinniss, M.: Incompatibility *In-Vitro* and *In Vivo* Demonstrated Only With Saline Suspended Red Cells. *Vox Sang*. *36. no.* 5: 301, May, 1979.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE<br>PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02002-05 BB |

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)
Use of Hepatitis B Immune Globulin Following Accidental Exposure to HBV

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Harvey G. Klein, M.D., Asst. Chief, Blood Bank Department, CC

Other: Harvey J. Alter, M.D., Chief, Immunology Section, Blood Bank, CC,
Paul V. Holland, M.D., Chief, Blood Bank Department, CC
David DeMets, Ph.D., Biometrics Researcher, National Heart, Lung and Blood Institute

COOPERATING UNITS (if any)

NHLBI

LAB/BRANCH
Blood Bank Department

SECTION
Immunology Section

INSTITUTE AND LOCATION
Clinical Center, Building, 10A, Room 1E33, NIH, Bethesda, Maryland 20205

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☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Two reported, randomized, double blinded trials have demonstrated the efficacy of high titer hepatitis B immune globulin (HBIG) in affording temporary passive immunity to individuals accidentally exposed to low doses of HBsAg-positive material. In both studies, a 5 ml injection of HBIG was given within one week of exposure and a second injection one month later. This two dosage schedule was chosen arbitrarily.

A single dose schedule of HBIG has proven efficacious in prophylaxis of spouses exposed to hepatitis B. However, the two dosage schedules, single injection and divided injection, have never been compared in a controlled study. This study enrolled individuals accidentally exposed to hepatitis B positive materials. Candidates were randomized in a double blinded fashion and treated with the same dose of HBIG in either a single or double injection. Two hundred and ninety-six individuals have been enrolled. Followup samples were collected at monthly intervals, following exposure, for six months and at 9 and 12 months.

Z01-CL-02002-05 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 - September 30, 1980

Project Title: Comparison of single dose and divided dose administration schedules of Hepatitis B immune globulin: Efficacy in preventing hepatitis B following accidental exposure (needle stick).

Previous Serial Number: Z01-CL-02002-04 BB

Principal Investigator: Harvey G. Klein, M.D.

Other: Harvey J. Alter, M.D.
Paul V. Holland, M.D.
David, DeMets, Ph.D.

Cooperating Units: NHLBI

Man Years: Total: 2
Professional: 1
Other: 1

## Project Description

### Objectives:

To determine whether a single injection of hepatitis B immune globulin (HBIG) is as effective as a divided dose injection in preventing hepatitis B caused by accidental exposure.

### Methods Employed:

Exposed individuals were referred by telephone to the Clinical Center Blood Bank. The purpose of the study was explained, and a telephone questionnaire used to determine eligibility for study.

Individuals who qualified were required to send blood specimens to the Blood Bank to assure exposure to an infectious source and susceptibility of the individual. Simultaneously, the individual was supplied with an informed consent form which further explained the purpose of the study.

Individuals were randomized in a double blinded fashion to the single injection or divided dose schedule. Each received the same total dose of HBIG. Serial blood samples were obtained and a follow-up questionnaire completed at month 6 and month 12.

## Major Findings:

Two hundred and ninety-six individuals have been entered, and 171 have completed the 12 month followup. The two injection regimen patient group experienced less hepatitis than the single injection group. HBsAg-positive "donor" samples have been tested for HBeAg and anti-HBe to see how these markers correlate with their infectivity.

## Significance to Biomedical Research and Programs of the Institute:

The Clinical Center Blood Bank has had a longstanding interest in the problem of viral hepatitis caused by blood and blood products. This study should (1) add further information about the natural history of hepatitis following HBIG administration, (2) answer the question of whether a single injection is as effective as a divided dose, a question of great practical importance, and (3) provide valuable serum samples for studying other markers of hepatitis and hepatitis infectivity.

## Proposed Course:

The study has been completed, but statistical evaluation has not been finished.

## Publications:

1. Klein, H.G., Alter, H.J., and Holland, P.V.: Post-exposure Immunoglobulin Prophylaxis of Hepatitis B; a Comparison of Two Dosage Schedules. Proc. of the Second UCSF Symposium on Viral Hepatitis. In Vyas, G.N., Cohen, S.N., and Schmid, R. (Eds.): Viral Hepatitis. Philadelphia, Franklin Institute Press, 1978, pp. 483-486.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02003-06 BB |

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)
Role of Hemagglutinating and IgE Penicillin Antibody in Donor Blood

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigators: Richard J. Davey, M.D., Chief, Laboratory Section, CCBBD
Mary H. McGinniss, AB(ASCP)SBB, Research Biologist, CCBBD

Other: Harvey J. Alter, M.D., Chief, Immunology Section, CCBBD

COOPERATING UNITS (if any)

LAB/BRANCH
Blood Bank Department

SECTION
Immunology Section

INSTITUTE AND LOCATION
Clinical Center, Building 10A, Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.5 | 0.5 | |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Several years ago it was reported by us that some patients on penicillin therapy, when transfused with donor blood containing hemagglutinating penicillin antibody, suffered an untoward reaction similar to anaphylaxis or serum sickness. We are attempting to establish a prospective, control study to determine if passively transferred anti-penicillin antibody can induce allergic manifestations in patients who are receiving penicillin or penicillin derivatives as part of their therapy. Donors will be screened for a history of penicillin hypersensitivity and their blood will be tested for anti-penicillin antibodies by hemagglutination and radioimmunoassay techniques. Recipients of blood from donors with a history of penicillin hypersensitivity will be followed for untoward reactions following penicillin therapy and will also be tested for IgG and IgE anti-penicillin antibodies. Appropriate controls will be similarly followed. Approximately 80 units of blood have been screened and followed. The protocol will be completed when 100 units have been studied.

Z01-CC-02003-06 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 - September 30, 1980

Project Title: Passive Transfer of Penicillin Hypersensitivity in Transfused Blood

Previous Serial Number: Z01-CC-02003-05 BB

Principal Investigators: Richard J. Davey, M.D.
Mary H. McGinnis, AB(ASCP)SBB

Other Investigators: Harvey J. Alter, M.D.

Cooperating Units: Inside NIH
None

Outside NIH
None

Man Years: Total: 0.5
Professional: 0.5
Other: 0

## Project Description

### Objectives:

A. To study the incidence and type of untoward reaction patients on pencillin therapy may experience when transfused with blood from a donor having a history of penicillin allergy and/or hemagglutinating or IgE penicillin antibody.

B. To gather data on the number of NIH donors having these types of antibodies and to do a statistical analysis on the data.

### Methods Employed:

1. All donors will be questioned regarding a history of penicillin allergy. Those with such history will be divided into those with anaphylactic reactions and those with just rash. The next consecutive donor after the donor giving a positive history of penicillin allergy will serve as a control.

2. An aliquot of serum will be obtained from both allergic and control patients and the aliquot tested for IgM, IgG (hemagglutination) and IgE (RAST) anti-penicillin antibody.

3. Recipients of blood from allergic and control patients will be followed for untoward reactions occurring within 48 hours of transfusion. Such reactions will be correlated with whether or not the recipient is being treated with penicillin or a penicillin derivative.

4. Pre- and post-transfusion samples will be obtained from those recipients who received blood from a donor with detectable anti-penicillin antibody to determine if passive transfer can be documented.

## Major Findings:

In 1971, at the American Association of Blood Banks meeting, we reported findings in three patients on penicillin suffering untoward reactions which retrospectively could only be attributed to the passive infusion of penicillin antibody in donor blood. This was the impetus for the present study.

In the original study, of 29 patients who received a unit(s) of blood known to contain hemagglutinating penicillin antibody, three (10%) had untoward reactions of the serum sickness variety which could not be attributed to any other factor.

Subsequently 9 new cases of possible urticaria or serum sickness type of reactions following blood transfusion to patients receiving penicillin have been observed. A causal relation between donor anti-penicillin antibody and recipient reaction has, however, been difficult to document because the radioimmunoassay for IgE anti-penicillin antibodies is not working optimally.

Approximately 80 units from donors with a history of an allergic reaction to penicillin in the past ten years have been identified. These units have been tested for IgG and IgE penicillin antibodies and randomly transfused. Preliminary analysis of the data suggests that no untoward reactions have occurred in recipients of these units.

## Significance to Biomedical Research and the Program of the Institute:

A. Identification of another possible cause of untoward reaction of blood transfusion.

B. If it can be shown that some penicillin reactions in patients are due to passive transfer of anti-penicillin antibody, then such patients will not need to be restricted from future penicillin therapy.

C. Similary, if it can be shown that such a mechanism for penicillin reactions exists, then patients being treated with penicillin will have to receive blood from donors without a history of penicillin allergy and/or without demonstrable anti-penicillin antibodies.

Proposed Course:

Approximately 100 units from penicillin-sensitive donors will be tested and followed. At that point the study will be terminated, the data analyzed, and conclusions drawn.

Publications: None

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02005-11 BB |

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)
Prospective Study of Post-transfusion Hepatitis (PTH) in Open Heart Surgery Patients

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Harvey J. Alter, M.D., Chief, Immunology Section, CCBBD

Others: Paul V. Holland, M.D., Chief, Clinical Center Blood Bank Department
Robert H. Purcell, M.D., Head, Hepatitis Virus Section, LID, NIAID

COOPERATING UNITS (if any)
NIAID, NHLBI

LAB/BRANCH
Blood Bank Department

SECTION
Immunology Section

INSTITUTE AND LOCATION
Clinical Center, Building 10A, Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 12 | 4 | 8 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Prospectively follow adult patients undergoing open heart surgery for the development of post-transfusion hepatitis and by appropriate serologic tests to determine the causative agents. Investigate the incidence of non-A, non-B hepatitis to see if there are any epidemiologic or serologic clues to its prevention. This study compares the clinical course of the various forms of PTH to determine the frequency with which chronic hepatitis develops.

Z01-CL-02005-11 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 - September 30, 1980

Project Title: Prospective Study of Posttransfusion Hepatitis (PTH) in Open Heart Surgery Patients

Previous Serial Number: Z01-CL-02005-10 BB

Principal Investigator: Harvey J. Alter, M.D.

Other Investigators: Robert Purcell, M.D.
Paul V. Holland, M.D.

Cooperating Units: Inside NIH
NIAID, NHLBI

Outside NIH
None

Man Years: Total: 12
Professional: 4
Other: 8

## Project Description

Objectives:

1. To prospectively follow adult patients undergoing open heart surgery at NIH for evidence of PTH.

2. To determine the relative occurrences of type B, type A and type non-A, non-B hepatitis.

3. To determine the effectiveness of various tests for HBsAg for screening blood donors.

4. To compare the clinical course of the various forms of PTH and to determine the frequency with which chronic hepatitis develops.

5. To develop improved screening methods for type B and type non-B hepatitis.

Methods:

1. All adult patients undergoing open heart surgery are followed for six to nine months with serial tests for ALT, HBsAg and anti-HBs.

2. Cases of hepatitis are additionally tested for serologic response to CMV, EBV and the hepatitis A virus; if type B disease, they are tested for anticore antibody, e antigen, DNA polymerase and subtype of HBsAg.

3. Donors are tested by the most sensitive methods for HBsAg currently available. In addition donors are tested for ALT to see if this relates to recipient hepatitis.

Major Findings: Studies to date have demonstrated:

1. The increased risk of blood containing HBsAg.

2. A 90% reduction in hepatitis by exclusion of commercial and HBsAg positive donors.

3. The superiority of RIA over CEP as a donor screening method for HBsAg carriers.

4. The fact that approximately 90% of PTH is now due to a previously unrecognized virus (or viruses) currently termed "non-A, non-B."

5. That type A hepatitis virus is almost never implicated in PTH: neither have the CMV or EBV been implicated in our cases.

6. That non-A, non-B heptitis is generally less acutely severe than type-B disease but the former frequently tends to become chronic.

Significance to Biomedical Research and the Program of the Clinical Center:

These studies have been instrumental in establishing many key points concerning the frequency, etiology, and prevention of PTH at the Clinical Center and across the United States.

Proposed Course: See objectives and methods.

Publications:

Holland, P.V., Alter, H.J., Purcell, R.H., Walsh, J.H., Morrow, A.G., and Schmidt, P.J.: The Infectivity of Blood Containing the Australia antigen. In Prier, J.E. and Friedman, H. (Eds.): Australia Antigen. Baltimore, University Park Press, 1973, p. 205-211.

Alter, H.J., Holland, P.V., Purcell, R.H., Lander, J.J., Feinstone, S.M., Morrow, A.G., and Schmidt, P.J.: Posttransfusion Hepatitis after Exclusion of the Commercial and Hepatitis B Antigen Positive Donor. Ann. Int. Med. 77: 691-699, 1972.

Feinstone, S.M., Kapikian, A.Z., Purcell, R.H., Alter, H.J., and Holland, P.V.: Transfusion-associated Hepatitis Not Due to Viral Hepatitis Type A or B. N. Eng. J. Med. 292: 767-770, 1975.

Alter, H.J...., Holland, P.V., and Purcell, R.H.: The Emerging Pattern of Post-transfusion Hepatitis. *Am. J. Med. Sci.* 270: 329-334, 1975.

Alter, H.J., Purcell, R.H., Holland, P.V., Feinstone, S.M., Morrow, A.G., Moritsugu, Y.: Clinical and Serological Analysis of Transfusion-Associated Hepatitis. *Lancet* 2: 838-481, 1975.

Alter, H.J., Purcell, R.H., Feinstone, S.N., Holland, P.V., Morrow, A.G.: Non-A, Non-B Hepatitis: A Review and Interim Report of an Ongoing Prospective Study. Proc. of the Second UCF Symposium on Viral Hepatitis In Vyas, G.N., Cohen, S.N. and Schmid, R. (Eds.): *Viral Hepatitis*, Philadelphia, Franklin Institute Press, 1978, pp. 359-369.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NOTICE OF
INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01-CL-02010-06 BB

PERIOD COVERED

October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

Chronic Sequelae of Non-A, Non-B Hepatitis

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Jay Hoofnagle, M.D., Senior Investigator, NIAMDD

Others: Harvey J. Alter, M.D., Chief, Immunology Section, Blood Bank Department, CC
Robert H. Purcell, M.D., Head, Hepatitis Virus Section, LID, NIAID
Anthony Jones, M.D., Chief, Section on Diseases of the Liver, DDB, NIAMDD
Kamal Ishak, M.D., Armed Forces Institute of Pathology

COOPERATING UNITS (if any)

NIAID, NIAMDD, AFIP

LAB/BRANCH

Blood Bank Department

SECTION

Immunology Section

INSTITUTE AND LOCATION

Clinical Center, Building 10A, Room 1E33, NIH, Bethesda, Maryland 20205

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| TOTAL MANYEARS: 2 | PROFESSIONAL: 2 | OTHER: |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

All patients developing non-A, non-B hepatitis following open heart surgery will be followed with serial studies of ALT to determine the incidence of chronic liver disease and to compare this incidence with those having type B hepatitis. Liver biopsy will be obtained when the ALT is elevated for more than 6 months and then again at one and three years. Biopsy material will be obtained for fluorescent and EM studies, as well as light microscopy with multiple stains.

Z01-CL-02010-06 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 - September 30, 1980

Project Title: Chronic Sequelae of Non-A, Non-B Hepatitis

Previous Serial Number: Z01-CL-02010-05 BB

Principal Investigator: Jay Hoofnagle, M.D.

Other: Harvey Alter, M.D.
Robert Purcell, M.D.
Anthony Jones, M.D.
Kamal Ishak, M.D.

Cooperating Units: Inside NIH
NIAID, NIAMDD

Outside NIH
Armed Forces Institute of Pathology

Man Years: Total: 2
Professional: 2

## Project Description

Objectives:

1. To follow-up patients identified as having non-A, non-B hepatitis post-transfusion.
2. To determine by ALT the frequency and persistence of chronic hepatitis.
3. To determine by liver biopsy the histologic pattern of non-A, non-B hepatitis and to save biopsy specimens for immunofluorescent and EM studies.
4. To elucidate the natural history of chronic non-A, non-B hepatitis.

Methods Employed: See objectives

Major Findings:

Chronic hepatitis frequently follows acute non-A, non-B hepatitis. In the patients thus far biopsied the histologic picture is similar to chronic type B hepatitis, showing features of either chronic persistent or chronic active hepatitis.

Significance to Biomedical Research and the Program of the Clinical Center:

Non-A, non-B hepatitis now accounts for 80% to 90% of PTH and is thus a major transfusion hazard. While it tends to be less acutely severe than type B hepatitis, preliminary evidence suggests that it progresses to chronic hepatitis with considerable frequency. Very little is known about this disease and it is imperative that clinical and serologic studies be undertaken. It is possible that a high percentage of idiopathic chronic active hepatitis and cryptogenic cirrhosis is due to the chronic sequelae of previously unrecognized non-A, non-B hepatitis.

Proposed Course: See objectives

Publications:

1. Berman, M., Alter, H.J., Ishak, K.G., Purcell, R.H., and Jones, E.A.: The Chronic Sequelae of Non-A/Non-B Heptitis. Annals of Int. Med. 91: 1-6, 1979.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02011-06 BB |

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)
The Duffy Blood Group Determinant and Susceptibility to Malaria

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Louis H. Miller, M.D., Head, Malaria Section, LPD, NIAID

Others: Mary H. McGinniss, AB(ASCP)SBB, Research Biologist, Clinical Center, Blood Bank
Paul V. Holland, M.D., Chief, Blood Bank Department, Clinical Center

COOPERATING UNITS (if any)
Laboratory Parasitic Diseases, NIAID

LAB/BRANCH
Blood Bank Department

SECTION
Immunology Section

INSTITUTE AND LOCATION
Clinical Center, Building 10A, Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2 | 2 | |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Working with an in vitro model for invasion of red cells by malaria merozoites, this study has demonstrated that human red cells lacking the Duffy a and b antigens are resistant to invasion. This corresponds well with epidemiologic studies which show that approximately 70% of West African and American blacks are resistant to Vivax malaria. A similar proportion of these blacks are Duffy a and b negative whereas the Duffy negative genotype is extremely rare in other racial groups. The close association between the Duffy negative and resistance to Vivax malaria has been confirmed by retrospective analysis of 11 volunteers experimentally inoculated with P. vivax. A retrospective study of U.S. servicemen who contracted malaria in South East Asia has been completed and again confirmed our original hypothesis. A second study conducted by the CDC in Honduras has also been completed and is another in vivo study in-proof.

Z01-CL-02011-06 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 - September 30, 1980

Project Title: The Duffy Blood Group Determinant and Susceptibility to Malaria

Previous Serial Number: Z01-CL-02011-05 BB

Principal Investigator: Louis H. Miller, M.D.

Other: Mary H. McGinniss, AB(ASCP)SBB
Paul V. Holland, M.D.

Cooperating Units: Lab. Parasitic Disease, NIAID

Man Years: Total: 2
Professional: 2

## Project Description

### Objectives:

A. To use a red cell culture technique to determine if invasion of erythrocytes by *Plasmodium falciparum* is dependent upon antigenic determinants on the erythrocyte membrane similar to that found for *P. vivax* malaria.

B. To characterize the antigens involved and determine the sequence of events when malarial invasion occurs.

C. To determine if RBC antigens are involved in other, less known forms of malaria and other parasitic diseases using the RBC as part of its life cycle.

### Methods Employed:

1. *P. falciparum* merozoites are added to RBC in culture and the degree of RBC invasion is observed microscopically. The degree of invasion of RBC with differing phenotypes is compared.

2. When a specific antigen is identified as being involved in the attachment or invasion by malaria parasites (as in (1)), attempts are made to block or destroy that site with specific antibody or enzyme treatment.

3. Blood samples from donors of rare MNS system phenotypes are being collected to test with *P. falciparum* parasites.

## Major Findings:

Last year, one cell among many tested was not invaded normally by P. falciparum parasites. This was a very rare cell known as En(a-). Repeat testing did not enhance our feeling that this cell might hold the clue to a red cell invasion receptor. Instead, we have shifted to testing various trypsin treated cells because this treatment, of itself, reduces invasion of cells by 50-75%. One cell, when trypsin treated, a S neg s neg U neg cell, showed 95% reduction of invasion; therefore, we suspect that S or s antigens might be involved. Work is continuing using rare red cells which genetically lack these antigens or do not express these antigens adequately.

A new finding concerning P. vivax is that anti-$Fy^3$, in addition to anti-$Fy^a$ and $Fy^b$, when added to $Fy^a$ or $Fy^b$ positive cells, will block invasion of P. vivax merozoites. This confirms our latest hypothesis that the invasion receptor is not $Fy^a$ or $Fy^b$, per se, but rather is an, as yet, unidentified part of the Duffy molecule.

## Significance to Biomedical Research and the Program of the Institute:

A. Elucidation of the mechanisms of red cell invasion by P. falciparum.

B. Increased knowledge of erythrocyte polymorphisms.

C. Accumulation of data which could culminate in a vaccine or other immunologic means of malaria prevention.

## Publications

1. Miller, L.H., Mason, S.J., Dvorak, J.A., McGinniss, M.H., and Rothman, I.K.: Erythrocyte Receptors for Plasmodium knowlesi Malaria: The Duffy Blood Group Determinants. Science. 159: 561-563, 1975.

2. Miller, L.H., Mason, S.J., Clyde, D.F., and McGinniss, M.H.: The Resistance Factor to Plasmodium vivax in Blacks. N. Eng. J. Med. 295: 302-304, 1976.

3. Miller, L.H., Haynes, J.D., McAuliffe, F.M., Shiroishi, T., Durocher, J.R., and McGinniss, M.H.: Evidence for Differences in Erythrocyte Surface Reeptors for the Malarial Parasites. Plasmodium falciparum and Plasmodium knowlesi. J. Exp. Med. 146: 277-281, 1977.

4. Mason, S.J., Miller, L.H., Shiroishi, T., Dvorak, J.A., and McGinniss, M.H.: The Duffy Blood Group System and Susceptibility to Plasmodium knowlesi Malaria. Brit. J. Haem. 36: 327-335, 1977.

5. Miller, LH., McGinniss, M.H., HOlland, P.V., and Sigmon, P.: The Duffy-Group Phenotype in American Blacks Infected with Plasmodium vivax in Vietnam. Am. J. of Trop. Med. and Hyg. 27: 1069-1072, 1978.

6. Spencer, H.C., Miller, L.H., Collins, W.E., Knud-Hansen, C., McGinniss, M.H., Shiroishi, T., Labos, R.A., and Feldman, R.A. The Duffy Blood Group and Resistance to *Plasmodium vivax* in Honduras. *Am. J. Trop. Med. and Hygiene*. 27: 664-670, 1978.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02013-04 BB |

PERIOD COVERED
October 1, 1979 - June 30, 1980

TITLE OF PROJECT (80 characters or less)
Mechanism of Vertical Transmission of Hepatitis B Virus

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: George Grady, M.D.

Others: Harvey J. Alter, M.D., Chief, Immunology Section, Blood Bank Department, Clinical Center

COOPERATING UNITS (if any)
Massachusetts Department of Public Health

LAB/BRANCH
Blood Bank Department

SECTION
Immunology Section

INSTITUTE AND LOCATION
Clinical Center, Building 10A, Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
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| 1 | 0.5 | 0.5 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Maternal-fetal transmission is felt to be responsible for a large number of chronic carriers of HBsAg. The mechanism by which the virus is transmitted from mother to infant, is, however, unclear with the three main possibilities being: (1) transplacental transmission prior to birth, (2) swallowing of maternal blood at the time of delivery, and (3) post-partum transmission via breast feeding or maternal handling.

We will attempt to differentiate each of these possibilities by delivering infants of HBsAg-positive chimpanzees by Caesarian section and by having each infant reared separate from its HBsAg-positive mother.

Z01-CL-02013-04 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

NIH-PHS
Individual Project Report
October 1, 1979 - June 30, 1980

Project Title: Mechanism of Vertical Transmission of Hepatitis B Virus

Previous Serial Number: Z01-CL-02013-03 BB

Principal Investigator: George Grady, M.D.

Other: Harvey J. Alter, M.D., CCBBD

Cooperating Units: Massachusetts Department of Public Health

Man Years: Total: 1
Professional: .5
Other: .5

## Project Description

1. To see if maternal-fetal hepatitis B transmission occurs despite the absence of any post-partum contact between mother and infant.

2. To see if the possibility of blood ingestion by the fetus can be avoided by bloodless Caesarian section and to see what impact this has on maternal-fetal transmission of hepatitis B virus.

3. To see if prepartum transmission can be documented by the presence of HBsAg in cord blood or by the presence of hepatitis related antigens in fetal liver tissue obtained at the time of delivery.

## Methods:

1. Chronic HBsAg carrier chimpanzees will be housed and bred in the Laboratory for Experimental Medicine and Surgery (LEMSIP). The carriers employed will be e antigen positive to document their potential infectivity.

2. Chimps will be delivered by as atraumatic and bloodless Caesarian section as possible.

3. At birth, samples will be obtained for HBsAg and e antigen testing from maternal blood, cord blood, fetal venous blood and amniotic fluid. A liver biopsy will also be obtained from the fetus and stained by fluorescent techniques for the presence of HBcAg and HBsAg.

4. The fetus will have no contact with the HBsAg-positive mother after delivery and will be followed for the development of type B hepatitis.

Major Findings:

The first infant so studied developed type B hepatitis seven weeks after delivery. This rules out post-partum contact as the cause of hepatitis transmission, but does not distinguish the other possibilities because the Caesarian section was not entirely bloodless. Against transplacental transmission, was the finding of HBsAg-negative cord blood and fetal venous blood. However, liver biopsy was not performed at the time of birth.

Significance to Biomedical Research and the Program of the Clinical Center:

It has been estimated that maternal-fetal transmission of hepatitis B is the major cause for the development of the HBsAg carrier state. Throughout the world this is probably a far more significant route of transmission than blood transfusion. Any studies which elucidate the mechanism of such transmission may help in its prevention. It has already been proposed that mothers who are HBsAg-positive be delivered by Caesarian section. These studies may shed light on the rationale for such an approach.

Proposed Course:

The carrier mother whose fetus has already been followed will be impregnated as soon as possible and the second fetus delivered by a more meticulous C-section. Liver biopsy at the time of delivery will be performed on the newborn.

Publications: None

| SMITHSONIAN SCIENCE INFORMATION EXCHANGE<br>PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02014-04 BB |
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PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)
Transmission of Non-A, Non-B Hepatitis to Chimpanzees

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Harvey J. Alter, M.D., Chief, Immunology Section, CCBBD

Others: Robert H. Purcell, M.D., NIAID
Paul V. Holland, M.D., Chief, CCBBD

COOPERATING UNITS (if any)
NIAID

LAB/BRANCH
Blood Bank Department

SECTION
Immunology Section

INSTITUTE AND LOCATION
Clinical Center, Building 10A, Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2 | 1 | 1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Ninety percent of post-transfusion hepatitis now appears related to a third human hepatitis "virus" tentatively termed "non-A, non-B." There are several pieces of evidence to suggest this is a virus, but to date this agent has not been observed, has not had a reproducible antigenic marker, and has not been observed, has not been grown in culture. This study will attempt to identify bloods with a high probability of containing virus and will inoculate chimpanzees. If chimpanzees are infected, they will be observed for the development of chronic hepatitis, will be reinoculated to stimulate antibody responses, and will be cross challenged to determine if there is more than one non-A, non-B agent.

PHS-6040
(Rev. 10-76)

Z01-CL-02014-04 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 - September 30, 1980

Project Title: Transmission of Non-A, Non-B Hepatitis to Chimpanzees

Previous Serial Number: Z01-CL-02014-03 BB

Principal Investigator: Harvey J. Alter, M.D.

Other: Robert Purcell, NIAID
Paul V. Holland, CCBBD

Cooperating Units: NIAID

Man Years: Total: 3
Professional: 1.5
Other: 1.5

## Project Description

### Objectives:

1. To prove that non-A, non-B hepatitis is due to a transmissible agent (or agents).
2. To transmit the virus of NANB from humans to chimpanzees and, if successful, from chimpanzee to chimpanzee.
3. To obtain plasmapheresis units from infected chimpanzees to aid in characterization of the virus and development of serologic tests.
4. To determine if more than one agent of non-A, non-B hepatitis exist.

### Methods:

1. Potentially infectious serums will be obtained from patients with acute and chronic non-A, non-B hepatitis and from donors implicated in such transmission.
2. Depending on the volume of sample available, from 1 ml to 75 ml will be inoculated into chimpanzees and the animals followed for six months for evidence of enzyme elevations.
3. Animals with elevated AST/ALT will be plasmapheresed and have liver biopsies. Biopsy material will be observed for evidence of hepatitis; it will also be examined by immunofluorescence and electronmicrography.

4. Acute phase plasma from reactive chimps will be administered to additional animals in an attempt to demonstrate serial passage.

5. Infected chimps will be rechallenged with the same inoculum to boost antibody response.

6. Following 5, chimpanzees will be cross challenged to determine by cross immunity if there is more than one agent of non-A, non-B hepatitis.

7. Partial hepatectomy may be performed in infected chimps to serve as a source of non-A, non-B antigen.

Major Findings:

Serums were obtained from four patients with well documented non-A/non-B hepatitis and from one donor implicated in non-A/non-B transmission. These were inoculated into five chimpanzees and all five showed biochemical and histologic evidence of acute hepatitis. This study demonstrated two major points: (1) non-A/non-B hepatitis is due to a transmissible agent and (2) there is a chronic carrier state in humans for the non-A, non-B agent(s) just as there is for the type B agent. The latter is based on the fact that transmission occurred following inoculation of plasma obtained from patients with chronic as well as acute non-A/non-B hepatitis.

Three serial passages have been documented in chimpanzees. Booster experiments have been done but the samples have not been analyzed for antibody.

Proposed Course:

Additional chimps may be inoculated using serums derived from patients whose incubation period suggests a second non-A, non-B agent. Cross challenge experiments will also proceed in an attempt to define if there is more than one non-A, non-B agent.

Publications:

1. Alter, H.J., Purcell, R.H., Holland, P.V. and Popper, H: Transmissible Agent in "Non-A, Non-B" Hepatitis. Lancet 1: 459-463, 1978.

2. Shimizu, Y.K., Feinstone, S.M., Purcell, R.H., Alter, H.J., and London, W.T.: Non-A, non-B hepatitis: Ultrastructural Evidence for Two agents in Experimentally Infected Chimpanzees. Science 205: 197200, 1979.

| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02[illegible] BB |
|---|---|---|

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)
Evaluation of Anti-Core Antibody and Serum Transaminase Tests as Indicators for the Infectivity of HBsAg-Negative Donors

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Harvey J. Alter, M.D., Chief, Immunology Section, CCBBD

Others: Paul V. Holland, M.D., Chief, Blood Bank Department, CC
Deloris Koziol, Medical Research Technologist, Blood Bank Department, CC

COOPERATING UNITS (if any)

LAB/BRANCH
Blood Bank Department

SECTION
Immunology Section

INSTITUTE AND LOCATION
Clinical Center, Building 10A, Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.5 | 0.5 | 1 |

CHECK APPROPRIATE BOX(ES)
☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Despite sensitive radioimmunoassay tests for HBsAg applied to all donor blood, some type B hepatitis continues to occur following transfusion. It has previously been suggested that HBsAg-negative individuals that have anti-core antibody may transmit the hepatitis B virus. The availability of a new sensitive radioimmunoassay for anti-core antibody allows this postulate to be tested in our prospectively followed, open heart surgery patients. Similarly, we can ascertain if chronic carriers of non-A, non-B hepatitis have elevated levels of serum transaminase and, if so, whether this could be employed to screen donors and reduce the frequency of post-transfusion hepatitis due to this agent.

Z01-CL-02016-04 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 - September 30, 1980

Project Title: Evaluation of Anti-Core Antibody and Serum Transaminase as Indicators of the Infectivity of HBsAg-Negative Donors

Previous Serial Number: Z01-CL-02016-03 BB

Principal Investigator: Harvey J. Alter, M.D.

Other: Paul V. Holland, M.D.
Deloris Koziol, Medical Research Technologist

Cooperating Units: None

Man Years: Total: 1.5
Professional: 0.5
Other: 1

## Project Description

### Objectives:

1. To determine if HBsAg-negative donors who have anti-core antibody are more likely to transmit type B hepatitis than those who lack anti-core antibody.

2. To determine if donors with elevated ALT are more likely to transmit non-A, non-B hepatitis than donors with normal ALT and to ascertain if this would be a practical way to screen for chronic carriers of this presumed virus.

### Methods:

1. We have now prospectively followed almost 600 patients to determine if they developed post-transfusion hepatitis and, if so, by what etiologic agent. All donors to type B and non-A, non-B hepatitis cases will be tested for anti-core antibody as will the donors to at least 30 patients who did not develop hepatitis (approximately 500 donors in all). Data will be analyzed to see if there is any positive correlation between the presence of anticore antibody in the donor and hepatitis in the recipient.

2. All donors to open heart surgery patients will be tested for ALT. These tests will be performed in a sample obtained at the time of donation but will not be tested until approximately three days after transfusion. The results of transaminase tests will not be known at the time of transfusion, but recipients will be followed prospectively for the development of

hepatitis. Data will be analyzed to see if there is a positive correlation between the presence of elevated donor transaminase and the development of recipient hepatitis.

3. When an elevated transaminase is found (initially tested under contract by Bionetics Lab), the same sample will be retested by the Clinical Chemistry lab at NIH. If the elevated value is confirmed and hepatitis occurs in the recipient, the donor will be recalled and at least two units of plasma obtained by plasmapheresis for subsequent attempts to isolate a non-A, non-B agent.

Major Findings:

Donors with elevated levels of ALT are more likely to cause NANB viral hepatitis in recipients of their blood than area donors with normal levels of ALT. Donors with anti-core antibody without concomitant anti-HBs may be carriers of the hepatitis B virus but the low frequency of hepatitis B occurring after transfusions at the CC makes data collection slow.

Significance to Biomedical Research and the Program of the Clinical Center:

Any test system which could reliably detect carriers of hepatitis B who are below the detectability range of RIA tests for HBsAg or which would detect chronic carriers of non-A, non-B virus would have an impact on the incidence of post-transfusion hepatitis.

| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02017-04 BB |
|---|---|---|

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)
Identification of the Non-A, Non-B Hepatitis Agent and the Development of Serologic Markers

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Harvey J. Alter, M.D., Chief, Immunology Section, CCBBD

Others: Robert Purcell, M.D., NIAID
Stephen Feinstone, M.D., NIAID
John Gerin, Ph.D., Georgetown University

COOPERATING UNITS (if any)
Laboratory Infectious Disease, NIAID
Georgetown University

LAB/BRANCH
Blood Bank Department

SECTION
Immunology Section

INSTITUTE AND LOCATION
Clinical Center, Building 10A, Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2 | 1 | 1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A non-A, non-B antigen will be sought in serums from patients with acute or chronic non-A, non-B hepatitis by reacting them with convalescent phase serums in assays. In addition, plasma units derived from: either donors implicated in non-A, non-B hepatitis or patients with acute or chronic non-A, non-B hepatitis will be ultracentrifuged. The pellet derived by ultracentrifugation will be reacted against a radiolabelled IgG fraction obtained from patients convalescent from non-A, non-B hepatitis in a solid phase radioimmunoassay system.

PHS-6040
(Rev. 10-76)

Z01-CL-02017-04 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 - September 30, 1980

Project Title: Identification of the Non-A, Non-B Hepatitis Agent and the Development of Serologic Markers

Previous Serial Number: Z01-CL-02017-03 BB

Principal Investigator: Harvey J. Alter, M.D.

Others: Robert Purcell, NIAID
Stephen Feinstone, NIAID
John Gerin, Georgetown University

Cooperating Units: NIAID, Geogetown University

Man Years: Total: 2
Professional: 1
Other: 1

## Project Description

### Objectives:

1. To obtain a large quantity of non-A, non-B hepatitis viral antigen.

2. To establish a sensitive detection system for this presumed viral agent.

### Methods:

1. Semi-purify non-A, non-B viral antigen by ultracentrifugation of plasma units clinically presumed to carry this agent.

2. Prepare radiolabelled IgG from plasma of persons who have recovered from non-A, non-B hepatitis in the hopes that they contain specific antibody.

3. React the antigen and antibody in a solid phase radioimmunoassay system.

4. If an assay can be developed, the antigen pellet will be further purified by cesium chloride and sucrose gradients.

### Major Findings:

Five plasma units have thus far been ultracentrifuged and found negative. Additional plasma units will be investigated as will acute and chronic phase serum samples.

Proposed Course: See objectives and methods

Significance to Biomedical Research and the Program of the Clinical Center:

The development of a detection system for non-A, non-B viral agent(s) would be highly significant in that none are currently available and in that this agent(s) currently is responsible for over 90% of post transfusion hepatitis and probably responsible for a great deal of chronic active hepatitis.

Publications: None

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02018-04 BB |

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)
Hepatitis B Vaccine Trial Among Renal Dialysis Patients

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Wolf Szmuness, M.D., Chief, Epidemiology, New York Blood Center

Others: Cladd Stevens, M.D., New York Blood Center
Edward Harley, New York Blood Center
Harvey J. Alter, M.D., Chief, Immunology Section, CCBBD

COOPERATING UNITS (if any)
New York Blood Center

LAB/BRANCH
Blood Bank Department

SECTION
Immunology Section

INSTITUTE AND LOCATION
Clinical Center, Building 10A, Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 6 | 2 | 4 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A two part study is being undertaken to evaluate a hepatitis B vaccine being produced by NIAID. In the first phase baseline seroepidemiologic data was obtained in 10 dialysis units in New York Blood Center and the Metropolitan Washington Renal Dialysis Unit. When the hepatitis B vaccine became available (approximately Fall 1979) a prospective, controlled, randomized double blind trial of its efficacy was started in these same dialysis units.

Z01-CL-02018-04 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 - September 30, 1980

Project Title: Hepatitis B Vaccine Trial Among Renal Dialysis Patients

Previous Serial Number: Z01-CL-02018-03 BB

Principal Investigator: Wolf Szmuness, M.D.

Others: Cladd Stevens, M.D., New York Blood Center
Edward Harley, New York Blood Center
Harvey J. Alter, M.D., Clinical Center Blood Bank Department

Cooperating Units: New York Blood Center

Man Years: Total: 6
Professional: 2
Other: 4

## Project Description

### Objectives:

1. To obtain baseline incidence figures on hepatitis B and non-A, non-B among a large number of renal dialysis patients and staff.

2. To try to assess patterns of hepatitis spread in these units based on serologic and epidemiologic criteria.

3. To evaluate the effectiveness of a hepatitis B vaccine in reducing the frequency of type B hepatitis among patients and staff.

### Methods:

1. Patients and staff in multiple dialysis units will be monitored monthly for evaluation of ALT and appearance of HBsAg and anti-HBs. More frequent sampling and additional tests such as those for subtyping, e antigen and anti-core antibody will be employed when a positive result is obtained.

2. When the hepatitis B vaccine is ready for clinical trials, patients and staff of these dialysis units will be randomly assigned to receive hepatitis B vaccine or placebo and the effectiveness of each assessed over a one year period in each individual. The hepatitis B vaccine will be prepared from a purified preparation of 20 nm HBsAg-containing particles which have been formalin treated and which have already been shown to be non-infectious, but immunogenic, in chimpanzees. Patients and staff will be monitored as above.

3. Other potential methods of decreasing the risk of hepatitis will also be employed including the administration of HBIG to those accidentally inoculated with HBsAg-positive material and the isolation of positive patients as recommended by the CDC.

4. All serologic and epidemiologic data will be computerized.

## Major Findings:

The preliminary epidemiology phase is completed and has been used for the design and implementation of the vaccine study which is underway.

## Significance to Biomedical Research and the Program of the Clinical Center:

Dialysis patients and staff remain a very high risk population for hepatitis B and represent one of the few US populations in which a hepatitis vaccine can be clinically evaluated. If the vaccine proves effective, it will have vast implications, not only for dialysis patients and staff, but also for patients and staff in institutions, for medical personnel in general, for inner city and sexually promiscuous populations, and for many foreign populations where hepatitis B frequencies are extremely high.

**Proposed Course:** See methods and objectives.

**Publications:** None

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02019-04 BB |

PERIOD COVERED

October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

Evaluation of the Hepatitis Risk of Hospitalized Patients Undergoing Invasive Procedures, but not Receiving Blood Transfusion

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Harvey J. Alter, M.D., Chief, Immunology Section, CCBBD

Others: Paul V. Holland, M.D., Chief, Blood Bank Department, CC
Robert H. Purcell, M.D., Head, Hepatitis Virus Section, LID, NIAID

COOPERATING UNITS (if any)

NIAID, NHLBI

LAB/BRANCH

Blood Bank Department

SECTION

Immunology Section

INSTITUTE AND LOCATION

Clinical Center, Building 10A, Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 3.5 | 0.5 | 3 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

This is a study which will serve to supplement and control project Z01-CL-02005-10 BB. Cardiac patients will be enrolled if they undergo closed mitral commissurotomy or cardiac catheterization but do not receive blood. They will then be followed prospectively for 6 months and hepatitis rates compared with patients undergoing open heart surgery. This should provide data on the relative risk of hepatitis between transfusion exposure and exposure to a hospital environment and the types of hepatitis associated with each.

PHS-6040

Z01-CL-02019-04 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 - September 30, 1980

Project Title: Evaluation of the Hepatitis Risk of Hospitalized Patients Undergoing Invasive Procedures, But Not Receiving Blood Transfusion

Previous Serial Number: Z01-CL-02019-03 BB

Principal Investigator: Harvey J. Alter, M.D.

Others: Paul V. Holland, M.D.
Robert Purcell, M.D.

Cooperating Units: NIAID, NHLBI

Man Years: Total: 3.5
Professional: 0.5
Other: 3

## Project Description

### Objectives:

1. To determine if there is a viral hepatitis risk which accompanies hospitalization and invasive procedures such as closed mitral commissurotomy and cardiac catheterization.

2. To compare this hepatitis risk with patients with similar cardiac lesions who require transfusion as part of corrective surgical procedures for their cardiac lesion.

3. To determine the type of viral hepatitis in each group (i.e. B versus non-A, non-B) and thus to establish the absolute incidence of non-A, non-B hepatitis related to blood transfusion.

### Methods:

1. All patients undergoing closed mitral commissurotomy or cardiac catheterization (with or without coronary angiogram) will be followed for six months with serial tests for ALT, HBsAg and anti-HBs.

2. Patients who develop hepatitis will be additionally tested for serologic responses to CMV, EBV and the hepatitis A virus; if type B disease, they will be additionally tested for anti-core antibody, e antigen and will be subtyped.

Major Findings:

Approximately 1% of subjects enrolled to date have developed evidence of viral hepatitis.

Significance to Biomedical Research and the Program of the Clinical Center:

This study will serve as a control for project No. Z01-CL-02005-10 BB and will define the baseline hepatitis incidence which accompanies hospitalization and invasive procedures not accompanied by blood transfusion.

Proposed Course: See objectives and methods

Publications: None

| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01- [illegible] |
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PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)
Alterations in Whole Blood Oxygen Affinity Following Transfusion

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Harvey G. Klein, M.D., Asst. Chief, Blood Bank Department, CC

Other: Robert M. Winslow, M.D, Senior Investigator, National Heart, Lung and Blood Institute

COOPERATING UNITS (if any)

NHLBI

LAB/BRANCH
Blood Bank Department

SECTION
Blood Services Section

INSTITUTE AND LOCATION
Clinical Center, Building 10A, Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2 | 1 | 1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

It has been widely reported that whole blood oxygen affinity varies in different disease states characterized by anemia. The fact that whole blood oxygen affinity is reduced in persons with sickle cell anemia has been known for many years. There is very little quantitative information concerning serial changes in whole blood $O_2$ affinity post-transfusion in thos disease states which require transfusion of red cells. It is quite possible that post-transfusion changes in $O_2$ affinity actually result in a more severe functional anemia despite the hemoglobin elevation. If the red cell milieu is important, whole blood O2 affinity post-transfusion may differ significantly in such different disease states as thalassemia, sickle cell anemia, aplastic anemia and myeloid metaplasia. In this study, whole blood O2 affinity will be measured in patients who require transfusion (1) prior to transfusion, (2) daily for 5 days, and (3) weekly thereafter for three weeks. Whole blood oxygen affinity of the transfused blood will be measured as well. A quantitative estimate of the percent of transfused cells remaining in each sample will be derived by differential agglutination (Ashby technique).

Z01-CL-02020-04 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 - September 30, 1980

Project Title: Alterations in Whole Blood Oxygen Affinity Following Transfusion

Previous Serial Number: Z01-CL-02020-03 BB

Principal Investigator: Harvey G. Klein, M.D.

Other: Robert M. Winslow, M.D.

Cooperating Units: NHLBI

Man Years: Total: 2
Professional: 1
Other: 1

## Project Description

### Objectives:

1. Determine what alterations occur in whole blood oxygen affinity and 2,3 DPG following transfusion.

2. Determine whether any changes in oxygen affinity occur in the transfused red cells which might suggest an influence of the "disease milieu."

3. Determine whether such changes vary according to the blood product transfused (fresh blood, bank blood, frozen blood).

4. Follow these alterations as the transfused red cells are eliminated from the recipient's circulation.

5. Exercise patients pre- and posttransfusion to determine physiological correlation with changes in $O_2$ affinity.

### Methods Employed:

Patients who require transfusion on the Molecular Hematology Service will be studied. The studies will initially be confined to patients with thalassemia, sickle cell anemia and aplastic anemia. Initially patients of blood group A, B or AB will receive group O ("universal donor") packed red cells. A five cc pretransfusion specimen as well as a five cc aliquot from the transfused cells will be obtained for measurements of whole blood oxygen affinity and 2,3 DPG levels. Whole blood $O_2$ affinity will be measured by the technique of

Rossi-Bernardi. A one hour posttransfusion specimen, daily specimen for five days and weekly specimens for three weeks will be drawn. Percent of transfused cells remaining will be measured by differential agglutination (Ashby technique) and correlated with changes in $O_2$ affinity. Additionally the recipient's cells will be lysed in vitro by use of an anti-A or anti-B hemolysis. This will permit separation of transfused from recipient cells in the posttransfusion specimen. Oxygen affinity can then be determined directly on the remaining transfused cells and on the whole blood. These determinations permit calculation of $O_2$ affinity of the lysed recipient cells. In this way it should be possible to determine whether specific changes occur in the transfused cells population post-transfusion and what component is the major influence in changes in whole blood $O_2$ affinity.

A second series of studies using ABO identical transfusions of red cells and whole blood can be carried out if donor and recipient are not identical for a minor blood group. This is necessary to permit separation of donor from recipient cells following transfusion. For these studies, differences in the presence of red cell M antigen will be used to distinguish donor from recipient cells. This antigen was chosen because of its low immunogenicity, rarity of clinical importance of anti-M isoantibodies, and presence of an anti-M reagent potent enough to effect the required separation.

Major Findings:

In sickle cell disease, changes in flow characteristics which result from exchanging AA cells for SS cells are more important in determining $O_2$ delivery than are shifts in the oxygen dissociation and 2,3 DPG levels.

Significance to Biochemical Research and the Program of the Clinical Center:

This project has practical importance in the management of blood resources and the transfusion approach for chronic anemia. Results of these studies should indicate the physiologic changes that result in different anemia states when various red cell preparations are transfused.

Proposed Course:

This study should have its initial phase completed within one year.

Publications: none

| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02022-03 BB |
|---|---|---|

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)
Identification of Bacterial Organisms with Human Red Cell Antigen Specificity

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigators: Mary H. McGinniss, AB(ASCP)SBB, Research Biologist
Paul V. Holland, M.D., Chief, Blood Bank Department, CC

Other: James D. MacLowry, M.D., CC, CP, Deputy Chief

COOPERATING UNITS (if any)
Clinical Pathology

LAB/BRANCH
Microbiology

SECTION

INSTITUTE AND LOCATION
Clinical Center, Building 10A, Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2 | 2 | |

CHECK APPROPRIATE BOX(ES)
☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Bacterial organisms are being analyzed for inhibitory property for red cell antibody and ability to confer red cell antigens on red cells negative for those antigens.

The red cells of patients with positive blood cultures are being analyzed for acquisition of non-genetically determined red cell antigens.

Z01-CL-02022-03 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 - September 30, 1980

Project Title: Identification of Bacterial Organisms with Human Red Cell Antigen Specificity

Previous Serial Number: Z01-CL-02022-02 BB

Principal Investigators: Mary H. McGinniss, AB(ASCP)SBB
Paul V. Holland, M.D.

Other: James D. MacLowry, M.D.

Cooperating Units: Inside NIH
Microbiology Service, Clin. Path. Dept., CC

Outside NIH
None

Man Years: Total: 2
Professional: 2

## Project Description

### Objectives:

A. To identify bacteria with red cell antigen-like specificity.

B. To search for acquisition of non-genetic antigens in septicemic patients.

### Methods Employed:

1. Bacterial cultures, whole and sonicated, plus their filtrates are being analyzed for their ability to inhibit antibodies and adsorb to human red blood cells.

2. Patients with bacterially proven sepsis will have their red cells phenotyped for the presence of non-genetic red cell antigens. This will require phenotype of pre-sepsis red cells and/or phenotype of family members, if available.

### Major Findings:

One patient, with D-strep sepsis, developed an acquired Kell antigen. Sonicated organisms from this patient had the ability to turn Kell negative cells, Kell positive *in vitro* and the whole organisms turned JK(b-) cells to JK(b+).

Another patient, with P. mirabilis infection, made an auto anti-JKb causing a brisk hemolysis in vivo. P. mirabilis organisms will confer JKb-like specificity to JK(b-) cells in vitro.

Significance to Biomedical Research and the Program of the Institute:

A. Elucidation of a previously known phenomenon by which patients may develop allo- or autoantibodies to red cell antigens which may restrict the availability of crossmatch compatible blood.

B. Biochemical analysis of organisms with specificity similar to red cell antigens may aid in understanding the biochemistry of single red cell antigen specificities.

C. Understanding of red cell antigens in health and disease whereby these usually genetically controlled characteristics may be lost or acquired in certain clinical situations.

Publications: None

|  |  |  |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-C[illegible]-0[illegible]3-[illegible] |

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)
Blood Group Substances in Malignant and Benign Breast Cyst Fluids

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Mary H. McGinniss, AB(ASCP)SBB, Research Biologist,
Clinical Center Blood Bank Department

Other: Ernest V. DeMoss, M.D., Surgical Branch, NCI

COOPERATING UNITS (if any)

NCI

LAB/BRANCH
Surgical Branch, NCI

SECTION

INSTITUTE AND LOCATION
Clinical Center, Building 10, NCI

|  |  |  |
|---|---|---|
| TOTAL MANYEARS: 1 | PROFESSIONAL: 1 | OTHER: |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Breast cyst fluids are being analyzed for the presence of soluble blood group substances, both serologically and biochemically. These data will be correlated, at a later date, with breast cyst fluid analysis for malignancy. If a consistent difference is noted between malignant and non-malignant cyst fluids, it may serve as a marker for patients at risk.

Z01-CL-02023-03 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 - September 30, 1980

Project Title: Blood Group Substances in Malignant and Benign Breast Cyst Fluids

Previous Serial Number: Z01-CL-02023-02 BB

Principal Investigator: Mary H. McGinniss, AB(ASCP)SBB

Other Investigators: Ernest V. DeMoss, M.D.

Cooperating Units: Inside NIH
NCI

Outside NIH
None

Man Years: Total: 1.0
Professional: 1.0
Other: 0

## Project Description

### Objectives:

A. To delineate any differences in soluble blood substances found in breast cyst fluid from malignant tissue as opposed to benign tissue.

B. To test the accuracy of anti-T titers to predict breast malignancy as opposed to benign breast cysts.

### Methods Employed:

1. Breast cyst fluids, supplied by Dr. DeMoss of the NCI Surgical Branch, will be tested using an inhibition test, for the presence or absence of $Le^a$, $Le^b$, A, B, H, M, N and T soluble substances.

2. Blood serum from the patients will be tested for atypical red cell antibodies and anti-T titer.

3. Saliva from these patients will be tested for secretor status (ABH) and Lewis substance.

4. Red cells will be used for a complete red cell phenotype.

Major Findings:

Cyst fluids from 16 patients have been studied. Three fluids appeared to inhibit an anti-T reagent. One patient had a significantly low titer of anti-T in her serum and her cyst fluid partially inhibited the anti-T reagent. Serum has not been obtained yet on two of the three patients whose cyst fluid inhibited the anti-T reagent. The third had a normal and anti-T titer.

Work is continuing using a modification of the method used to date for cyst fluids. Cyst fluids will now be boiled to destroy enzymes which may inactivate blood group substances and they will also be filtered to render them free of cellular debris. These data will be correlated soon with cytology data. Work will continue until 50 patients' cyst fluids have been analyzed.

Significance to Biomedical Research and the Program of the Institute:

A. If a consistent difference is noted between malignant and nonmalignant cyst fluids, it may serve as a marker for patients at risk.

B. Anti-T titers could become part of a breast cancer work-up.

Proposed Course:

To analyze, as stated above, 50 patients who are admitted for aspiration of breast cyst fluid.

Publications: None

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02024-03 BB |

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)
Frozen Red Cells in Prevention of Non-A/Non-B Hepatitis

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Harvey J. Alter, M.D., Chief, Immunology Section, CCBBD

Others: Robert Gerety, BOB, FDA
Leonard Seeff, VA, Washington, D.C.
George Grady, State Lab, Boston, Massachusetts

COOPERATING UNITS (if any)
VA Hospital, Washington, D.C.
State Lab, Boston, Massachusetts

LAB/BRANCH
Blood Bank Department, Clinical Center; Bureau of Biologics, Bethesda, Maryland

SECTION
Immunology Section

INSTITUTE AND LOCATION
Clinical Center, Building 10A, Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 3 | 1 | 2 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

It has been suggested in the literature, but never conclusively documented, that frozen-deglycerolized red cells (FDRC) could prevent post-transfusion hepatitis (PTH). In a recent experiment, we showed in a chimpanzee model that FRBC did not prevent the development of type B PTH. Since 80-90% of PTH is now due to the non-A/non-B agent or agents it seems appropriate to determine if FRBC play any role in prevention of this disease. Such a study has now become feasible because of the recent transmissions of non-A/non-B hepatitis to chimpanzees. In this study, we will utilize whole blood from a donor shown to transmit non-A, non-B hepatitis to both humans and chimpanzees. The blood will be frozen and deglycerolized by standard techniques and then tested for infectivity in chimpanzees.

Z01-CL-02024-03 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 - September 30, 1980

Project Title: Frozen Red Cells in Prevention of Non-A/Non-B Hepatitis

Previous Serial Number: Z01-CL-02024-02 BB

Principal Investigator: Harvey J. Alter, M.D.

Other: Robert Gerety, BOB, FDA
Leonard Seeff, M.D., VA, Washington, D.C.
George Grady, M.D., State Lab, Boston, Mass.

## Project Description

1. To procure whole blood units known to contain an infectious inoculum of the non-A/non-B hepatitis agent.

2. Units will be subjected to a standard method of freezing and deglycerolization.

3. Frozen and deglycerolized cells and appropriate controls will be inoculated into chimpanzees who will be followed for biochemical and histologic evidence of viral hepatitis.

## Methods:

1. Whole units of blood will be obtained from a donor known to transmit non-A/non-B hepatitis. In addition, a large volume of infectious plasma will be obtained by plasmapheresis.

2. Freezing and deglycerolization will be performed by a standard procedure for human use employing the IBM red cell washer.

3. Chimpanzees will be transfused with frozen deglycerolized cells and followed with weekly AST/ALT. Biopsies and plasmapheresis units will be obtained when indicated.

4. Chimpanzees who do not become infected will be tested for susceptibility to the non-A/non-B agent by subsequent inoculation with the untreated infectious plasma pool.

Major Findings: None to date

Proposed Course: See Objectives

## Significance to Biomedical Research and the Program of the Institute:

There is considerable uncontrolled data in the literature to suggest that FRBC prevent PTH. If true, this would provide a means of preventing PTH irrespective of our ability to detect virus in the donor. However, a previous chimpanzee study in our laboratory demonstrated that FRBC did not prevent type B PTH. Since 80-90% of posttransfusion hepatitis is now classified as non-A/non-B, it is important to establish if freezing and deglycerolization might prevent this form of hepatitis.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL [illegible] BB |

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)
Chronic Transfusion with a Fraction of Young Normal Red Cells (Neocytes)

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigators: Harvey G. Klein, M.D., Asst., Chief, CCBBD
Lawrence Corash, M.D., Hematology Section, CPD, CC

Others: Arthur Nienhuis, M.D., Chief, Clinical Hematology Branch, NHLBI
Albert Deisseroth, M.D., Chief, Experimental Hematology Section, PCP, NCI

COOPERATING UNITS (if any)
NHLBI and NCI

LAB/BRANCH
Blood Bank Department/Clinical Pathology Department

SECTION
Blood Services Section

INSTITUTE AND LOCATION
Clinical Center, Building 10A, Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2.5 | 1 | 1.5 |

CHECK APPROPRIATE BOX(ES)
☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)
The major complication of chronic red cell transfusion is hemosiderosis. One approach to limiting iron infusion is to lengthen the interval between transfusions. Although normal red cell survival is about 110 days, the average unit of blood contains cells of all ages, some of which survive only a few days post-transfusion. If one could prepare a unit containing only young red cells (neocytes), transfusion requirements might be halved. We have used an IBM 2997 cell separator to harvest a cohort of young cells (average age 15-30 days by pyruvate kinase analysis). These cells are frozen and deglycerolized for transfusion into chronically transfused thalassemic patients. To date $^{51}$Cr survival data suggest that neocytes circulate up to twice as long as frozen red cells. Clinical status of seven thalassemic patients supported on neocytes for two years, will be monitored. Part II of this protocol involves removal of senesent red cells (gerocytes) by a similar cell separation technique.

Z01-CL-02025-02 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 - September 30, 1980

Project Title: Chronic Transfusion with a Fraction of Young Normal Red Cells (Neocytes)

Previous Serial Number: Z01-CL-02025-01 BB

Principal Investigator: Harvey G. Klein, M.D.
Lawrence Corash, M.D.

Others: Arthur Nienhuis, M.D.
Albert Deisseroth, M.D.

## Project Description

### Objectives:

1. Prepare frozen deglycerolized red cell units which contain red cells with an average age of 15-30 days.

2. Determine *in vivo* survival and function of these cells.

3. Follow the transfusion requirements of several chronically transfused patients whose baseline transfusion requirement is well established.

4. Determine the efficacy and practicality of using a continuous flow cell separator for partial exchange transfusion of selected fractions of red cells.

### Methods Employed:

1. Blood Bank donors are asked to undergo neocytopheresis on the IBM Cell separator, a procedure which lasts about four hours and results in the removal of approximately 50 gm of hemoglobin in a 500 ml. volume. Donors must pass all standards for both whole blood donation and plasmapheresis. The cell separator is adjusted to collect "neocytes," young red cells, just below the buffy coat. Donor white cells, platelets and iron stores are monitored.

2. The neocyte component is frozen and assayed for pyruvate kinase before and after the freeze-thaw process. Such units are transfused into informed, chronically transfused, thalassemic patients who have had appropriate baseline studies. Seven such patients will eventually be totally supported by neocytes.

## Significance to Biomedical Research and Programs of the Institute:

The Clinical Center has had a longstanding interest in the hazards of chronic transfusion and has supported the thalassemic patients studied for iron overload by the Clinical Hematology Branch, NHLBI. This protocol explores development of a new red cell component which should cut the danger of iron overload in chronically transfused patients by up to 50%. If the principle can be established, further technologic development could make this procedure a major step forward in chronic transfusion therapy.

## Proposed Course:

The initial phase should last two years.

## Publications:

1. Klein, H.G.: Neocytopheresis: Collection, Preparation and Preliminary Clinical Results, in Proceedings of the Red Cross Apheresis Symposium, Chicago, 1979, p. 88-96, American Red Cross Blood Services, Mid America Region.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02026-02 BB |

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)
Immune Complexes in Non-A, Non-B Hepatitis

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Jules Dienstag, M.D., Asst. Prof. of Medicine
Massachusetts General Hospital

Others: Harvey J. Alter, M.D., Chief, Immunology Section, CCBBD
Robert H. Purcell, M.D., Head, Hepatitis Virus Section, LID, NIAID

COOPERATING UNITS (if any)
NIAID

LAB/BRANCH
Blood Bank Department

SECTION
Immunology Section

INSTITUTE AND LOCATION
Clinical Center, Building 10A, Room 1E33, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS: 3 | PROFESSIONAL: 2 | OTHER: 1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

1. Test serums from patients with non-A, non-B hepatitis for presence of immune complexes by RAJI cell assay and compare with patients with other forms of viral hepatitis and with controls without hepatitis.

2. Isolate complexes from non-A, non-B patients with high level activity by RAJI assay; dissociate complex and test derived "antigen" and "antibody" for non-A, non-B specificity by solid phase radioimmunoassay.

Z01-CL-02026-02 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 - September 30, 1980

Project Title: Immune Complexes in Non-A, Non-B Hepatitis

Previous Serial Number: Z01-CL-02026-01 BB

Principal Investigator: Jules Dienstag, M.D.

Other Investigators: Harvey J. Alter, M.D.
Robert H. Purcell, M.D.

Cooperating Units: Inside NIH
NIAID

Outside NIH
Massachusetts General Hospital

Man Years: Total: 3
Professional: 2

## Project Description

### Objectives:

1. To determine if patients with non-A, non-B hepatitis have circulating immune complexes.

2. To isolate complexes by their attachment to RAJI cells.

3. To dissociate complexes in attempt to isolate specific antigen and/or antibody for non-A, non-B viral hepatitis agent(s).

4. Test antigen and/or antibody by radioimmunoassay against appropriate acute and chronic hepatitis serums and against control serums.

### Methods:

1. Immune complexes will be measured by RAJI cell assay.

2. Immune complexes will be dissociated by low acid/or high molarity and the antibody reacted against serums by solid phase radioassay.

### Major Findings:

Immune complexes have been found in the majority of patients tested to date who are acutely ill with non-A, non-B heptitis.

Significance to Biomedical Research and the Program of the Institute:

There is a pressing need for a serologic test for the non-A, non-B virus(es). This project provides a novel approach to isolate a potential non-A, non-B antigen or antibody.

Proposed Course:

See Objectives and Methods

Publications:

Dienstag, J.L., Bhan, A.K., Alter, H.J., Feinstone, S.M., and Purcell, R.H.: Circulating Immune Complexes in Non-A, Non-B Hepatitis: Possible Masking of Viral Antigen. Lancet i: 1265-1267, 1979.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NOTICE OF
INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01-CL-020[illegible]7-01 BB

ERIOD COVERED
July 15, 1980 - September 30, 1980

ITLE OF PROJECT (80 characters or less)
Evaluation of Hepatitis B Vaccine in the Prevention of Maternal-Fetal Transmission of the Hepatitis B Virus

AMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER ROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Harvey J. Alter, M.D., Chief, Immunology Section, Blood Bank Department, Clinical Center

Other: Cladd Stevens, M.D., New York Blood Center

OOPERATING UNITS (if any)
New York Blood Center

AB/BRANCH
Blood Bank Department

ECTION
Immunology Section

NSTITUTE AND LOCATION
Clinical Center, Building 10A, Room 1E33, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| OTAL MANYEARS: 1 | PROFESSIONAL: 0.5 | OTHER: 0.5 |

HECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

An HBsAg-positive, HBeAg-positive chronic carrier chimpanzee has transmitted HBV infection to two consecutive offspring. After her next delivery we will administer hepatitis B vaccine to the infant to determine if vaccine used in this setting can prevent maternal-fetal transmission of HBV.

Z01-CL-02027-01 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
July 15, 1980 - September 30, 1980

Project Title: Evaluation of Hepatitis B Vaccine in the Prevention of Maternal-Fetal Transmission of the Hepatitis B Virus

Previous Serial Number: None

Principal Investigator: Harvey J. Alter, M.D., Chief, Immunology Section, Blood Bank Department, Clinical Center

Other Investigators: Cladd Stevens, M.D.

Man Years: Total: 1
Professional: 0.5
Other: 0.5

## Project Description

### Objectives:

To prevent offspring of HBsAg-positive chimpanzees from becoming chronic HBV carriers using a vaccine.

### Methods:

1. Breed chronic HBsAg/HBeAg-positive chimp (Alcinda).

2. Administer hepatitis B vaccine to infant immediately after delivery.

3. Follow offspring for nine months to determine if hepatitis B develops.

**Findings:** Project just beginning.

### Significance to Biomedical Research and the Program of the Institute:

Only one animal is involved at present. This animal's past history of maternal-fetal transmission makes her a candidate to test the efficacy of hepatitis B vaccine in this study. If the vaccine appears effective, this would support the conduct of a controlled trial in humans.

| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02028-01 BB |
|---|---|---|

PERIOD COVERED
July 15, 1980 - September 30, 1980

TITLE OF PROJECT (80 characters or less)
A Chimpanzee Study to Evaluate Anti-Viral Therapy (Adenine Arabinoside) in the Amelioration of Chronic NANB Hepatitis

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT
Principal Investigator: Harvey J. Alter, M.D., Chief, Immunology Section, CCBBD

COOPERATING UNITS (if any)

LAB/BRANCH
Blood Bank Department

SECTION
Immunology Section

INSTITUTE AND LOCATION
Clinical Center, Building 10A, Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2 | 0.5 | 1.5 |

CHECK APPROPRIATE BOX(ES)
☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)
Chimpanzees with enzymatic and histologic evidence of chronic NANB hepatitis will be treated with adenine arabinoside. Serial liver function studies and liver biopsy material will be obtained for 6-12 months after treatment in an attempt to assess the effect of treatment of the chronic hepatitis per se. In addition, post-treatment serums will be inoculated into additional chimpanzees to assess infectivity in comparison with pre-treatment serums. It is possible that treatment with ameliorate infectivity without altering hepatic inflammatory disease.

Z01-CL-02028-01 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
July 15, 1980 - September 30, 1981

Project Title: A Chimpanzee Study to Evaluate Anti-Viral Therapy (Adenine Arabinoside) in the Amelioration of Chronic NANB Hepatitis

Previous Serial Number: None

Principal Investigator: Harvey J. Alter, M.D., CCBBD

Man Years: Total: 2
Professional: 0.5
Other: 1.5

## Project Description

### Methods:

1. Four to five chimpanzees with evidence of chronic hepatitis (greater than one year) will be entered into the study.

2. They will be treated with a single three week course of adenine arabinoside (dose to be determined).

3. Serum transaminase will be followed weekly for one year after treatment. Serial liver biopsies and plasmapheresis will be performed before and after treatment. These will be obtained weekly early in the course of therapy and then biweekly to monthly for six months.

4. A pre-serum and three month post-treatment serum will be used for infectivity studies. The post-serum will be inoculated into a colony born chimpanzee not previously used in NANB experiments and the chimp will be monitored for six months. If hepatitis does not develop, then the same chimp will be given pre-treatment plasma or serum and similarly monitored.

5. Pending the outcome, additional courses of ARA-A and/or interferon will be considered.

Major Findings: Study just being initiated.

### Significance to Biomedical Research and the Program of the Institute:

Studies in humans with chronic type B hepatitis, indicate that ARA-A and/or interferon can abrogate the infectivity of these carriers. The effect on the hepatitis per se is equivocal. No such studies have been performed on humans with NANB hepatitis, because there are no serologic markers with which to

monitor the outcome and because it is more logical to use this experimental therapy in a better defined entity such as type B hepatitis. Nonetheless, chronic hepatitis and the chronic carrier state are very major problems in NANB hepatitis. The availability of chimps with chronic NANB hepatitis allows for a tentative assessment of drug therapy in this situation. Although the effect on hepatitis per se will be uncontrolled, the effect on infectivity will be internally controlled and could provide meaningful information.

Proposed Course: See Methods

Publications: None

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02029-01 BB |

PERIOD COVERED
July 15, 1980 - September 30, 1980

TITLE OF PROJECT (80 characters or less)
Evaluation of Asymptomatic Blood Donors Found to Have Elevated Serum Transaminase (ALT) During Routine Screening

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Harvey J. Alter, M.D., Chief, Immunology Section, CCBBD

Others: Jay Hoofnagle, M.D., Hepatic Unit, NIAMDD
Paul V. Holland, M.D., Chief, Blood Bank Department, CC

COOPERATING UNITS (if any)
Liver Unit, NIAMDD

LAB/BRANCH
Blood Bank Department

SECTION
Immunology Section

INSTITUTE AND LOCATION
Clinical Center, Building 10A., Room 1E33, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS:<br>3 | PROFESSIONAL:<br>3 | OTHER: |

CHECK APPROPRIATE BOX(ES)
☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

During the course of blood bank screening, 2.5% of "normal" donors have been found to have an elevated ALT. These donors will continue to be identified as part of a protocol. In order to determine the significance of these abnormalities donors will be recalled for complete history and physical with emphasis on any non-viral causes for elevated transaminase. In addition, their ALT will be monitored monthly for six months and periodically thereafter. They will also undergo liver-spleen scan, gall bladder x-rays and ultrasound, upper GI and, pending their course and separate informed consent, they may undergo liver biopsy. Their elevation will be similar to that of patients who develop chronic NANB hepatitis after transfusion.

Z01-CL-02029-01 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
July 15, 1980 - September 30, 1981

Project Title: Evaluation of Asymptomatic Blood Donors Found to Have Elevated Serum Transaminase (ALT) During Routine Screening

Previous Serial Number: None

Principal Investigator: Harvey J. Alter, M.D., Chief, Immunology Section, Blood Bank Department, Clinical Center

Others: Jay Hoofnagle, M.D., Hepatic Unit, NIAMDD
Paul V. Holland, M.D., Chief, Blood Bank Department, Clinical Center

Cooperating Units: Inside NIH
NIAMDD, Liver Unit

Outside NIH
None

Man Years: Total: 3
Professional: 3

## Project Description

Methods Employed:

1. Recall all donors previously found to have elevated ALT and those identified in ongoing study.

2. Obtain weekly ALT four times.

3. If values still elevate, initiate the following:

    a. complete history and physical with stress on possible non-viral causes of elevated ALT.
    b. liver-spleen scan.
    c. upper GI series
    d. gall bladder series and ultra-sound
    e. serum copper and ceruloplasmin determinations
    d. tests for $\alpha$ 1-antitrypsin deficiency

4. Monitor ALT monthly for 6 months.

5. If ALT abnormal for greater than 6 months, perform liver biopsy under separate informed consent.

Major Findings: Study just being initiated.

Significance to Biomedical Research and the Program of the Institute:

The frequency, etiology, and clinical significance of persistently abnormal ALT in asymptomatic individuals and with no history of liver disease is unknown. This study will help to better define this occurrence and may serve as the baseline for some subsequent therapeutic intervention.

Publications: None

[illegible] PROJECT NUMBER (Do NOT use this space) | HEALTH, [illegible] PUBLIC HEALTH [illegible] NOTICE [illegible] INTRAMURAL RESEARCH PR[illegible] | [illegible] -02020-01 BB

PERIOD COVERED
February 1, 1980 - September 30, 1980

TITLE OF PROJECT (80 characters or less)
Comparison of Standard and Modified Skin Preparation for Blood Donation

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Paul L. Chandeysson, M.D., CCBBD

Others: Joseph C. Fratantoni, M.C., BB, DBBP
Harvey G. Klein, M.D., CCBBD
David DeMets, Ph.D., H, HV, BR
Frank G. Witebsky, M.D., CC, CP

COOPERATING UNITS (if any)

Bureau of Biologics

LAB/BRANCH
Blood Bank Department/Clinical Pathology Department, CC

SECTION
Blood Services Section

INSTITUTE AND LOCATION
Clinical Center, Building 10A, Room 1I:33, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS:<br>2 | PROFESSIONAL:<br>3 4 | OTHER:<br>1¼ |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

This project is designed to compare the effectiveness of the standard method of preparing the venipuncture site of blood donors with a simpler method which is less irritating to the skin, less expensive, and quicker. Blood drawn using both skin preparation methods will be cultured to determine if there is any difference in the rate of contamination. Normal healthy volunteers will be used as subjects.

Z01-CL-02030-01 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
February 1, 1980 - September 30, 1980

Project Title: Comparison of Standard and Modified Skin Preparation for Blood Donation

Previous Serial Number: None

Principal Investigator: Paul L. Chandeysson, M.D., CCBBD

Other: Joseph C. Fratantoni, M.D., BB, DBBP
Harvey G. Klein, M.D., CCBBD
David DeMets, Ph.D., H, HV, BR
Frank G. Witebsky, M.D., CC, CP

Cooperating Units: Inside NIH
Clinical Pathology, CC

Outside NIH
Bureau of Biologics

Man Years: Total: 2
Professional: 3/4
Other: 1-1/4

## Project Description

### Objectives:

This project is designed to compare the effectiveness of the standard method of preparing the venipuncture site of blood donors with a simpler method which is less irritating to the skin, less expensive, and quicker. Blood drawn using both skin preparation methods will be cultured to determine if there is any difference in the rate of contamination. Normal healthy volunteers will be used as subjects.

### Methods Employed:

1. For this project, donors to be phlebotomized for research or control specimens will be asked if their blood can be cultured to determine the effectiveness of the skin preparation technique. Those that consent will be randomized into one of two groups: the experimental group which will be drawn using the modified skin preparation, and the control group using the standard skin preparation.

2. After the skin is prepared, a 16 gauge phlebotomy set (butterfly) with a 5 ml plastic syringe attached will be used for the venipuncture and 5 ml of blood will be drawn into the syringe. The first 5 ml presumably contains most of the skin contaminants and may contain a small piece of skin cored out by the phlebotomy needle. The phlebotomy set will be detached and an 18 gauge needle attached to the syringe and the 5 ml of blood will be injected into a 100 ml blood culture bottle after the stopper is cleaned with 2% tincture of iodine and allowed to dry. The phlebotomy set will then be used to collect the research or control blood in the usual manner; either by attaching a collecting bag or by drawing blood directly into collection tubes.

3. The blood culture bottles will be incubated unvented at 35-37 C. On the seventh day they will be subcultured to three plates of appropriate media. One plate will be incubated an aerobically in a $CO_2$ incubator at 35-37 C; one plate will be incubated an aerobically at 35-37 C; and one will be incubated in room air at room temperature.

Major Findings: None to date.

Significance to Biomedical Research and the Program of the Institute:

The contamination rate for each group, experimental and control, will be calculated as the number of positive blood cultures divided by the number of blood cultures. The contamination rate reflects the contamination due to failure of the donor skin preparation plus the contamination in inoculating and processing the blood culture. Since the latter is the same for both groups, the difference in the experimentally determined rates of contamination reflects the difference in effectiveness of the skin preparations. Because of the rate of contamination is expected to be low, a large number of blood cultures must be drawn to detect a difference in the contamination rate between the control and the experiment group. A contaminated unit of blood is a great culture medium for bacteria; infusion of such a unit could result in devastating transfusion reactions. Identification of simple yet safe and effective means to prepare the skin will lessen the risk of contaminating the blood and decrease adverse effects on our blood donors.

Publications: None

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NOTICE OF
INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01-CL-02031-01 BB

PERIOD COVERED
July 1, 1980 - September 30, 1980

TITLE OF PROJECT (80 characters or less)
Clinical Evaluation of Platelet Concentrates Stored by Temperature Cycling

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Richard J. Davey, M.D., Chief, Laboratory Services, CCBBD

Other: Manley McGill, Ph.D., Cell Preservation Laboratory, Red Cross Blood Services Laboratory

COOPERATING UNITS (if any)
National Cancer Institute

LAB/BRANCH

SECTION
Blood Bank Department

INSTITUTE AND LOCATION
Clinical Center, Building 10A, Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.5 | 0.4 | 0.1 |

CHECK APPROPRIATE BOX(ES)
☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The ideal storage conditions for platelet concentrates have yet to be defined. Liquid phase storage at either 4$^{\circ}$C or 22$^{\circ}$C for up to 72 hours are the currently recommended methods for platelet preservation. Factors which may affect platelet yield or viability such as the pH of the suspending medium, centrifuge speed, and drug ingestion by the donor have been extensively studied with platelets stored at each of these temperatures. Investigators at the American Red Cross have recently defined a new "temperature cycled" method of storing platelets, with 4$^{\circ}$C storage interrupted every 12 hours with a 45 minute pulse of 37$^{\circ}$C storage. In vitro studies indicate that this storage method tends to maximize the advantages while minimizing the disadvantages of each of the standard 4$^{\circ}$C or 22$^{\circ}$C storage temperatures currently used. The present study is designed to evaluate the in vivo effectiveness of temperature cycled platelets versus 4$^{\circ}$C stored platelets in approximately 20 thrombocytopenic patients. Serial platelet counts and bleeding times will be obtained.

S-6040

Z01-CL-02031-01 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
July 1, 1980 - September 30, 1980

Project Title: Clinical Evaluation of Platelet Concentrates Stored by Temperature Cycling

Previous Serial Number: None

Principal Investigator: Richard J. Davey, M.D., Chief, Laboratory Section, Blood Bank Department, Clinical Center

Other: Manley McGill, Ph.D.

Cooperating Units: NCI, American Red Cross

Man Years: Total: .5
Professional: .4
Other: .1

## Project Description

### Objectives:

1. To evaluate the *in vivo* effectiveness in thrombocytopenic patients of temperature cycled platelets. Bleeding times and platelet increments will be employed.

2. To study whether platelets maintained *in vitro* by temperature cycling can be safely stored for 96 hours.

3. To evaluate the practicality and cost of using a temperature cycling incubator in normal blood bank operation.

4. To pool NIH data with data obtained at other cooperating institutions so that meaningful conclusions can be drawn regarding the efficacy of this platelet storage method.

### Methods:

Patients to be studied will be adults who have thrombocytopenia (platelet counts below 30,000/ul) resulting from a failure to produce platelets. Only patients who have shown that 20% or more of $4^{\circ}$ stored platelets have remained in their circulation for 24 hours will be included. This requirement is intended to exclude individuals alloimmunized by previous transfusions.

Patients who have massive bleeding, who have received drugs known to inhibit platelet function, who are recovering from bone marrow suppression, who have gross splenomegaly, who have bacterial sepsis or a body temperature greater than 101°F, or who have disseminated intravascular coagulation will be excluded from the study.

Each patient will receive 0.2 units per kilogram of body weight of platelet concentrate stored by temperature cycling. Venous blood platelet counts and template bleeding times will be performed pretransfusion, and four and 24 hours post-transfusion.

a. After collection and preparation, platelet concentrates will be stored in a Forma Model 3020 Incubator with a 4°C and 37°C air mode.

b. Storage will begin in the 4°C mode and concentrates will not be agitated during storage.

c. The incubator timer will be set to switch to the 37°C mode at 8 a.m. and 8 p.m. of each storage day and remain in a 37°C mode for 45 minutes. The incubator will automatically return to 4°C upon completion of a 45 minute 37°C cycle.

d. Concentrates will be transfused immediately after a 37°C cycle or following a 30 minute exposure to 37°C air when transfusions are required, after 48-96 hours of storage.

Major Findings:

Sufficient data have not been accumulated for analysis.

Significance to Biomedical Research and the Program of the Institute:

Platelets stored at either 22°C or 4°C have morphologic and functional "storage lesions" which are characteristic of each temperature. Although FDA regulations allow storage of platelets at these temperatures for 72 hours, it has been recommended that platelets not be stored at 4°C for more than 24 hours, and not be stored at 22°C for more than 48 hours because of these "storage lesions."

In vitro studies suggest that "temperature cycling" platelets minimizes the "storage lesions" seen with 4°C and 22°C storage. This may permit storage of platelets for longer than 72 hours, thus easing the platelet supply problems caused by outdated units. Patients may be able to receive a superior platelet product, and platelet donor recruitment will be simplified.

Proposed Course: See above.

Publications: None

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02032-01 BB |

PERIOD COVERED
June 23, 1980 - September 30, 1980

TITLE OF PROJECT (80 characters or less)
Survival of Transfused Red Blood Cells From Undercollected Units Stored in CPDA-1

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Richard J. Davey, M.D., Chief, Laboratory Section, CCBBD

Others: Bruce Lenes, M.D., Blood Bank Department, CC
Ernest Simon, M.D., CCBBD
David DeMets, Ph.D., National Heart, Lung and Blood Institute, NIH

COOPERATING UNITS (if any)
NHLBI

LAB/BRANCH

SECTION
Blood Bank Department

INSTITUTE AND LOCATION
Clinical Center, Building 10A, Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.8 | 0.4 | 0.4 |

CHECK APPROPRIATE BOX(ES)
☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The amount of whole blood which must be collected into a commercially prepared collection bag containing the usual amount of anticoagulant is 450 ml ± 45 ml. Units inadvertently collected in amounts less than this must be discarded. The purpose of this study is to investigate whether blood collected in a volume of 275 ml will have adequate survival when transfused. Blood will be intentionally undercollected, made into packed red cells, and stored in CPDA-1 anticoagulant the maximum time of 35 days. A small amount of red blood cells will then be labeled with $^{51}$Chromium and retransfused into the donor to determine the post-transfusion red cell survival. The post-transfusion survival of red cells inadvertently undercollected because of technical difficulties or donor reactions will also be investigated in this manner.

Z01-CL-02032-01 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Description
June 23, 1980 - September 30, 1980

Project Title: Survival of Transfused Red Blood Cells From Undercollected Units Stored in CPDA-1

Previous Serial Number: None

Principal Investigator: Richard J. Davey, M.D., Chief, Laboratory Section, Blood Bank Department, Clinical Center

Other: Bruce Lenes, M.D., Blood Bank Department, Clinical Center
Ernest Simon, M.D., Blood Bank Department, Clinical Center
David DeMets, Ph.D., National Heart, Lung and Blood Institute, NIH

Cooperating Units: None

Man Years: Total: .8
Professional: .4
Other: .4

## Project Description

### Objectives:

A. To evaluate post-transfusion survival of autologous red cells collected in a volume smaller than currently allowed, and stored for 35 days in CPDA-1 anticoagulant.

B. To evaluate the data generated by this study and, if appropriate, recommend changes in the current volume limits for an acceptable unit of blood.

### Methods Employed:

1. Phlebotomy and storage.
a. "Deliberate" undercollected units. Participants in the study must meet all the American Association of Blood Banks criteria for blood donation which pertain to the safety of the donor. Since the survival of autologous red cells varies considerably between individuals, each donor will serve as his own control. That is, he will donate a unit of normal volume (450 ml), and also a deliberately undercollected unit (275 ml). These donations will be at least eight weeks apart. Deliberately undercollected units will be drawn in approximately the same time (6-8 minutes) as a unit of normal volume by slowing the rate of phlebotomy. Units for autologous transfusion will be signed by the donor, made into packed red cells with a hematocrit of less than 80% within 24 hours, and stored without agitation at 4°C on a special shelf in the Blood Bank refrigerator.

b. "Inadvertant" undercollected units. When the collection of blood intended for volunteer donation is terminated at less than 405 ml because of a donor reaction or technical difficulties, the donor will be asked if he/she wishes to participate in the study. If so, the unit will be handled for autologous transfusion as described above.

2. $^{51}$Cr Red Cell Survival:

After 35 days of storage approximately 3 ml of packed red cells will be labeled with approximately 30 uCi of $^{51}$Cr. The labeled red cells will be infused, and samples taken at 5, 10, and 20 and 30 minutes through a butterfly needle, and at 24 hours and 48 hours. The early samples will be used to determine the 100% survival point (zero time), and the 24 hour and 48 hour samples will be used to establish post-infusion survival.

Major Findings:

Sufficient data have not been accumulated.

Significance to Biomedical Research and the Program of the Institute:

The standards of the Food and Drug Administration and the American Association of Blood Banks require that the volume of whole blood collected into commercially prepared collection bags containing the usual amount of (63 ml) CPDA-1 anticoagulant-preservative be 450 ± 45 ml. Because of variety of problems with the venipuncture and because of donor reactions, units which are less than 405 ml are inadvertently drawn almost 3% of the time. Since over 11 million units are donated a year in this country, over 300,00 units a year must be discarded because they are undercollected.

The scientific basis for the required limits of 450 ± 45 ml has not been established for the currently used anticoagulant-preservative CPDA-1. There is some evidence that units as small as 200 ml collected in an earlier anticoagulant, CPD, have normal post-transfusion survival. If this study confirms that "undercollected" units are satisfactory for transfusion, a large number of units currently being discarded will be salvaged for patient care.

Proposed Course: See above.

Publications: None

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE<br>PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-02033-01 BB |

PERIOD COVERED
January 2, 1980 - August 31, 1980

TITLE OF PROJECT (80 characters or less)
Collection of Blood Hematopoietic Stem Cells with the IBM 2997 and the Haemonetics Model 30 Cell Separators

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Theodore Spiro, M.D., Resident, Clinical Pathology Department, Clinical Center

Others: Harvey G. Klein, M.D., Asst. Chief, Blood Bank Department, CC
Neal Young, M.C., Clinical Hematology Branch, NHLBI

COOPERATING UNITS (if any)
Clinical Hematology Branch, NHLBI

LAB/BRANCH
Blood Bank Department/Clinical Pathology Department

SECTION
Blood Services Section

INSTITUTE AND LOCATION
Clinical Center, Building 10A, Room 1E33, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1 | 0.5 | 0.5 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The use of marrow-derived hematopoietic stem cells in the supportive care of cancer patients receiving high dose radiotherapy was first reported in 1959. Since that time, many authors have reported studies using intensive chemotherapy and/or radiotherapy followed by transfusions of autologous bone marrow derived stem cells. The rationale for such a therapeutic approach is that grafting of these stem cells allows higher, potentially curative, doses of anti-tumor therapy to be administered, doses which might otherwise prove lethal because of bone marrow toxicity. The fact that hematopoietic stem cells are known to circulate in the peripheral blood has caused several laboratories to begin evaluation of the collection techniques and the transplantation potential of these stem cells. This study will characterize the hematopoietic stem cell collection capacity of the IBM 2997 and the Haemonetics Model 30 cell separators by assaying the CFU-c, the granulocyte-macrophage-eosinophil precurser cell and the BFU-e, the erythroid equivalent. These stem cells have been selected for study because of their capacity to predict hematopoietic reconstitution after bone marrow transplantation.

Z01-CL-02033-01 BB
Blood Bank Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
January 2, 1980 - August 31, 1980

Project Title: Collection of Blood Hematopoietic Stem Cells with the IBM 2997 and the Haemonetics Model 30 Cell Separators

Previous Serial Number: 80-CC-54

Principal Investigator: Theodore Spiro, M.D., Resident, Clinical Pathology Department, Clinical Center

Other: Harvey G. Klein, M.D., Asst. Chief, Blood Bank Department, Clinical Center
Neal S. Young, M.D., Clinical Hematology Branch, NHLBI

Cooperating Units: Inside NIH
Clinical Hematology Branch, NHLBI

Outside NIH
None

Man Years: Total: 1
Professional: .5
Other: .5

## Project Description

### Objectives:

1. To quantitate the hematopoietic stem cell collection capacity of the IBM 2997 and the Haemonetics 30 cell separator.

2. To characterize morphologically the collected stem cells and to compare them to marrow stem cells which are known to possess transplantation capacity in man.

### Methods Employed:

Five donors will be phlebotomized once on the IBM 2997 and once on the Haemonetics 30 cell separators for a comparative study of the two machines. Each of these five donors will be requested to return on two separate occasions to undergo this procedure. Five additional donors will be phlebotomized on the IBM 2997 to characterize precisely collection conditions. Approximately 225 ml of blood will be obtained during the Haemonetics procedure. Efficacy of collection under several sets of gravitational force/flow conditions will be assayed by quantitating both the granulocyte-macrophage-

eosinophil stem cell (CFU-c), using a modified Robinson and Pike culture technique, and the erythroid burst forming cells. Characterization of CFU-c will be performed by a whole amount technique allowing morphological studies to be undertaken. The donor will be studied 24 hours and 168 hours (7 days) after each procedure in order to determine the capacity of the individual to reconstitute his circulating peripheral blood stem cell pool (in the event that it is depleted during the procedure).

Major Findings:

An insufficient number of studies have been completed to allow any preliminary conclusions to be drawn.

Proposed Course: See methods.

Significance to Biomedical Research and the Program of the Institute:

This study will characterize quantitatively and qualitatively the hematopoietic stem cell collection capacity of the IBM 2997 and the Haemonetics 30 cell separators. Such studies are required for the determination of the feasability of peripheral blood stem cell transfusions for patients requiring hematopoietic reconstitution.

Publications: None

October 1, 1979 to September [illegible]

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

CLINICAL PATHOLOGY DEPARTMENT

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October 1, 1979 to September [illegible], [illegible]

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH
CLINICAL CENTER

## CLINICAL PATHOLOGY DEPARTMENT

## I. DEPARTMENT MISSIONS AND GOALS

The Clinical Center Clinical Pathology Department missions and goals are:

1. To provide the optimum laboratory medicine support to patient-care physicians and their patients within the Clinical Center
2. To act as a consultant to patient-care physicians regarding the interpretation of laboratory data and patient care problems in hematology.
3. To educate and train clinical pathology residents, clinical associates, and visitors in laboratory medicine.
4. To conduct a program of research and development in the area of laboratory medicine.
5. To provide the optimum phlebotomy and sterile urine collection service for patients within the Clinical Center.

## II. DEPARTMENT ACTIVITIES

### A. Service Productivity

The Clinical Pathology Department performed 2,214,21[illegible] tests in FY-1980 which represents an increase of 220,977 tests or an [illegible] increase over FY-1979. The Resource Monitoring System average [illegible] workload index increased to 109 after remaining constant at [illegible] for both FY-78 and FY-79.

During the year, the Hematology Service conducted a Wednesday morning Hematology Clinic to evaluate larger numbers of Clinical Center patients. This Clinic has been a success and has allowed the Hematology Service to continue its major role as the hematology consultant to physicians and patients in the Clinical Center and to individuals with hematologic problems in the immediate community.

During the last year the Hematology Service has interpreted [illegible] 1925 bone marrow specimens. Over 50% of the samples included bone marrow biopsies; all samples included clot sections, iron stains and aspirate smears for patients in the Clinical Center (total slides examined >7700). A large number (450) of bone marrow specimens have been sent for consultation from the National Cancer Institute, various surrounding institutions, as well as from all over the country. This

year, the Hematology Service performed 15% of the bone marrows in the Clinical Center. These were obtained by the Hematology Service physicians as consultative procedures and were useful in determining diagnosis, coordination of protocols, staging of disease, and determination of specific therapy.

This year, the number of in- and out-patient consultations by the Hematology Service was 81 per month. As in prior years, these consultations require multiple visits and follow-up of the patient for evaluation of laboratory results over a long period of time.

B. Personnel

One Staff Physician joined the Microbiology Service as a replacement for Dr. Mary Smaron. Also one Senior Chemist (Dr. Mahalyi) and one Staff Associate (Dr. MacDonald Horne) joined the Hematology Service.

C. Presentations

The staff of the Clinical Patholology Department made 68 formal presentations at universities and various national and international meetings.

D. Formal Training Courses Completed by Staff

Sixteen Commissioned Officers participated in 30 formal training courses.

Ninety-eight Civil Service employees participated in 164 formal training courses.

## III. MAJOR PROGRESS

A. Service

A revision of the "Clinical Pathology and Blood Bank Guide" was coordinated by the Office of the Chief. This guide is provided to help patient-care physicians make best use of laboratory services. It was distributed in August 1980, and contains a Master Table of all laboratory tests available at NIH whether performed by the Clinical Pathology Department, Blood Bank Department, laboratories within the Institutes, or via contract.

The planning, design, and logistics for the new laboratory facilities in the Ambulatory Care Research Facility were coordinated by the Office of the Chief. A committee composed of a member of the senior staff and technical staff from each Service met regularly to define the needs of and make selections for the Department in the new Facility (ACRF). This committee will also coordinate all aspects of the move to the new Facility which is now scheduled for April 1981.

The implementation throughout the Department of the workload unit system designed by the College of American Pathologists was coordinated by the Office of the Chief. This system became fully operational in August 1980 and will provide a major management tool for the assessment of current personnel and for the assignment of new personnel in the future. In addition, the workload of this Department can now be compared wit 4,000 to 5,000 other laboratories which use this system in the United States.

The Department was inspected by the College of American Pathologists in May, 1980. All Phase II deficiencies were corrected but several Phase I deficiencies which involve space and constraint of the current facilities will be corrected when the Department moves to the Ambulatory Care Research Facility. The laboratory was accredited by the College of American Pathologists for a two year period.

The services of the Phlebotomy and Urine Collection Team now include routine and STAT blood drawing for service, drawing blood samples for research, drawing blood specimens for culture, obtaining blood specimens in timed sequence studies, obtaining blood specimens at the appropriate time for therapeutic drug monitoring, and collecting mid-stream clean voided urine specimens for culture. Several changes have been made in the Phlebotomy and Urine Collection Team to improve efficiency and enhance communication with the Nursing Service. Each team member is now assigned to specific Nursing Units for early morning blood drawing (one to three units each). Pocket beepers are now in use by the phlebotomists and specimen pickup employees. The beepers have cut down on delays, prevented wasted time and increased productivity by 50%. All of the policies and procedures of the Phlebotomy and Urine Collection Team have been reviewed, updated and improved by the Supervisor of the Phlebotomy Team. Phlebotomists are now provided with in-service education through seminars, lectures, and films.

Clinical Chemistry Service. The College of American Pathologists (CAP) workload system was instituted for the Chemistry Service. Adjustments in personnel were made among the groups in the Chemistry Service based on the workload monitoring system to improve efficiency and productivity.

During the past three years, all methods of the Chemistry Service have been rewritten, updated, and placed into a standard format. This significant project is now completed and each method will be reviewed each year and updated as needed.

Each senior staff member of the Chemistry Service now has technical support for method development. The technologists in technical support positions provide backup to the service labs when needed, but otherwise assist senior staff members in method development and evaluation and in their individual research projects.

A new Chief Technologist was selected to replace the former Chief Technologist who took a new position. The transition occurred smoothly, and the new Chief Technologist is functioning well.

The Clinical Chemistry Service continued to introduce new tests into the laboratory replacing those sent to outside laboratories. This results in high quality results, cost savings, and shorter turnaround times. This year, phenobarbital, phenytoin, primidone, carbamazepine, gamma glutamyl transferase, urine 17-hydroxycorticosteroids, and free T4 were brought in-house for a yearly cost savings of approximately $150,000. Determination of high density lipoproteins was also added to available tests done in-house. Progress was made toward offering Vitamin A and tests for determination of other retinoids, as well as copper and zinc levels. In addition, the following methods were scheduled for development during the coming Fiscal Year to be available when the laboratory moves to the ACRF: urinary cortisol, CEA, insulin, growth hormone, digoxin, tegretol, 17 ketosteroids, VMA, and heavy metals.

The hours of operation of the major high volume analytical instrument, SMAC, have been extended to weekday evenings and weekend mornings providing increased efficiency for the laboratory and more rapid turnaround of patient-care results. The Chemistry Service is now able to have results available by 11:00 a.m. in the Medical Information System (MIS) for a SMAC panel from a routine specimen drawn that morning. Changes were made in the procedures for handling specimens with STAT requests. The turnaround time for STAT results was monitored throughout the year, and now the Chemistry Service is able to consistently provide STAT results within 40 minutes after receipt of the specimen by the Chemistry Service.

A number of new analytical instruments were added to the Service. These included a replacement for the old SMAC, a second new SMAC, two new blood gas analyzers, a new atomic absorption spectrometer, a third generation DuPont Automatic Clinical Analyzer (ACA) for STAT assays, a high pressure liquid chromatograph for retinoids, a new visible and fluorescent scanning densitometer, a phase contrast polarizing microscope for urinary sediment analysis, and a new gamma counter which counts 4 tubes at a time. Also, an existing second generation DuPont ACA was updated from 30 to 60 test channels. The second SMAC is used for STAT requests and permits rapid turnaround of results more efficiently. Each of these analytical instruments was carefully evaluated before analyses were available.

The delta check function of the Honeywell Computer System was evaluated. New delta check limits were defined for each analyte, and this has now become part of routine quality control policies for the Chemistry Service. This then is an additional check against specimen mix-up.

During this year, the Hematology Service evaluated and implemented a new analytical system, the Coulter S Plus. This system performs seven parameters of the CBC as well as the platelet count on each sample. Two identical instruments have decreased the turnaround time for sample analysis in the laboratory to less than 45 minutes. It has also allowed the Hematology Service to have a backup system so that work in the Hematology laboratory can always be performed on the same analytical system.

Because of a program to use whole blood samples from most outpatients instead of fingerstick samples, space was freed up which was converted into a Special Hematology laboratory and an office for the Chief Medical Technologist of the Hematology Service. This arrangement places the Special Hematology closer to the Hematology Service laboratory and helps in both acquiring and sending laboratory data via computer. The Chief Medical Technologist has an office independent of the first floor laboratory which has increased her efficiency.

An interface for the two Coulter S Pluses has been designed and the program written. Implementation of this interface has facilitated the sending of data to the computer and, thus, to the clinician. This has decreased the turnaround time to get patient results to the wards. A new computer and keyboard will be designed to accommodate on-line characterization of differentials and will allow one technologist to certify both the differential and the complete blood count, thus reducing the amount of clerical work and time required to provide data to clinicians.

The Quality Control program has been expanded and revised. The Quality Control technologist has responsibility not only for instrumentation and automation but for Special Hematology, morphology and coagulation.

The rotation of the technical staff has been modified so that individual technologists can now rotate into the Special Hematology section, the Quality Control section and Coagulation section. This new rotation gives the technologists a wider range of technological expertise and creates for the Hematology Service a large core of more widely trained individuals which will allow for more flexible use of the technical staff.

Evaluation and utilization of the WYLBUR RIAPROG for calculations of serum and red cell folate, serum vitamin $B_{12}$, and serum ferritin levels have resulted in a marked reduction from approximately six hours of hand calculations to 20 minutes of computer calculations. In addition, the computer system also allows for a comparison of standard curves to previous standard curves and for determination of the standard error of the mean of these curves.

Evaluation of a fluorometric substrate system for the determination of heparin, antithrombin III, plasmin, and plasminogen was completed. This semi-automated system did not prove to be reliable or precise enough for clinical usefulness.

Two new tests, the $B_{12}$ binding protein determination and the hemoglobin $A_{1c}$ level, have been introduced to the Hematology Service and will be offered as routine tests to patients in the Clinical Center.

The French, American, and British Group (FAB) classification of acute leukemias has been introduced into the Hematology Service and to physicians in the Clinical Center. All bone marrows will be signed out using only the FAB classification.

Laboratory Computer Service. An improved format for reporting clinical pathology results has been developed, pilot tested, and put into weekly use for all current patients. The new report groups related tests together, presents results in a cumulative chronological arrangement for an entire year, and reduces the space required to summarize a patient's results. This will greatly facilitate the assessment of laboratory results for patient care and research.

The usefulness of a "large delta list" for monitoring serial changes in patient results to detect possible laboratory errors has been evaluated.

The Laboratory Computer Service has provided statistical and computer support to evaluate new analytical methodologies and calibrate reagents used in the clinical laboratory.

An interactive system to produce summaries of the patterns of Clinical Center bacterial resistance to antimicrobial agents has been developed. Summaries may be produced on the basis of the kind of bacteria, the body source of the bacteria, the date of isolation, and the patients from whom the bacteria were isolated.

A review of the needs of the Department for clinical laboratory computer services and the options for obtaining these services in the Ambulatory Care Research Facility has been carried out.

Microbiology Service. A new screening plate and broth (CAMPY agar and CAMPY thio) have been added to the laboratory's stool culture procedure. These media should enhance our recovery of Campylobacter fetus, an agent recently recognized as an important agent of diarrheal disease.

Sputum specimens are now screened for adequacy of quality before being processed for routine culture. This is done using a Gram smear to determine the quantity of squamous epithelial cells. Institution of this procedure has reduced time consuning work-up of many inappropriate specimens.

Evaluation of a new product, Flow N/F system, to be used in the identification of Gram negative nonfermentative bacilli has been very promising. It is anticipated that this miniaturized system will replace our current tube system, and shorten identification times by several days.

Evaluation of two commercially available kits for the grouping of beta hemolytic streptococci resulted in the selection of the Streptex kit.

This is an agglutination procedure using antibody coated latex particles and provides grouping information within a matter of hours.

A throat Gram smear to predict the presence or absence of Group A streptococci was evaluated. This investigation did not suggest that this would be a reliable test to offer as an adjunct to culture.

The Syva Emit procedure has been instituted in the laboratory to measure gentamicin and tobramycin serum levels. This procedure allows a turnaround time of approximately 15 minutes as opposed to the minimum of five hours required previously.

The MIS ordering screens for microbiology have been revised to make them easier to understand and to facilitate the ordering of appropriate procedures on particular specimen types.

The Service laboratory manuals have undergone continued revision and updating to increase their clarity for the bench technologists and to assure that they accurately reflect rapidly changing laboratory procedures.

Arrangements have been made with Gibco Diagnostics to provide us with susceptibility-testing plates configured in the same way as those we have been preparing in-house. If these plates, after evaluation, prove acceptable, their use will save technologists' time now required for plate preparation and quality control.

A fluorescent anti-nuclear antibody technique has been implemented in the Serology Section which will permit this test, which had previously been performed on contract to be done in-house.

The fluorescent treponemal antibody (FTA-Abs) test, which is a very low volume but complex test, is now being performed satisfactorily and more rapidly on contract.

B. Research and Development

The Office of the Chief completed the analyses of data from the 14-page pathology questionnaire which evaluated the relationships among space, personnel, and test volume in 50 different academic pathology departments. A manuscript has been submitted which contains the mean and median values for space, personnel, test volume, publications, and personnel with a variety of ratios and linear regression relationships which will be valuable to this department and other pathology departments in the country. These data are now being compared with similar data from pathology departments in private hospitals compiled by the College of American Pathologists.

In the Clinical Chemistry Service efforts to increase quality and efficiency continued through evaluation of various instruments, upgrading of analytical procedures, addition of backup methods, and development of new technologies. Utilizing the new atomic absorption spectrophotometer, an in-line automated dilution and sampling system

was developed which allows the assay of calcium, magnesium, and lithium in 1/3 to 1/2 the time previously required. A commericial method for free thyroxine assay was evaluated and modified to make it suitable for use in our laboratory.

Two automated dipstick readers were evaluated for accuracy and precision for the analytes of pH, glucose, protein, hemoglobin, bilirubin, and ketones using patient and contrived urine specimens. Since analytical discrepancies were found in both instruments and neither instrument improved either the quality or throughput of work, no purchase was made.

An assay for the determination of 17-hydroxycorticosteroids in urine using column separation of the steroids was evaluated and implemented for patient-care physicians in the Clinical Center. This assay was previously performed by a contract laboratory. In addition, an evaluation of methods for the determination of vanillylmandelic acid (VMA) and 17-ketosteroids in urine was begun.

A large-scale normal range/biological variation/methodological variation study involving 1200 NIH employees over 2-1/2 years was launched.

Developmental work on a method for retinoids was begun with the acquisition of a new HPLC. Similarly, efforts to develop methods for copper and zinc were begun using the new atomic absorption stectrophotometer.

The determination of thyroxine ($T_4$) was compared using three different analytical techniques; radioimmunoassay, EMIT and fluorescent immunoassay. The preliminary results from this study showed significant differences among the three methods with the EMIT system being low and fluorescent immunoassay being high. Additional studies are being done to define the optimum system.

A project to shorten and reoptimize the radioimmunoassay for CK-BB was completed with the development of an assay requiring only 4 hours' incubation (compared to 2 days) and having the same performance characteristics as the regular assay.

In collaboration with the Department of Thoracic Surgery NHLBI, the combined determinations of lactate dehydrogenase (LD)-isoenzymes and creatine kinase (CK)-isoenzymes have been evaluated in patients undergoing different types of cardiac surgery. Useful information has been provided for the diagnosis of MI and other complications in these patients. General medical patients have been studied as well. The improved reliability and diagnostic discrimination of the LD isoenzyme test has provided valuable diagnostic information in the detection of MI and other complications.

An agarose gel electrophoretic system for the determination of lipoproteins has been improved and applied in the study of serum samples from normal subjects and patients with dyslipidemias. Abnormal lipoprotein patterns characterized by the absence of lipoprotein fractions and by the presence of extra fractions have been demonstrated and associated with defined pathological conditions. All these patterns form a reference record for the diagnosis and evaluation of lipoprotein abnormalities in normal subjects and patients. Application of the test to the study of lipoprotein patterns in patients undergoing hemodialysis demonstrated an abnormal lipoprotein in the serum of these patients. This lipoprotein may be associated with the development of accelerated atherosclerosis in these patients.

The study of the application of the radioimmunoassay of the BB isoenzyme of creatine kinase (CK-BB) to the diagnosis of patients with gastrointestinal and genitourinary cancers, especially prostatic cancer, was completed. Work on evaluation of the role of CK-BB in following the course of these patients and the comparison of CK-BB to other tumor markers such as CEA in prostatic cancer is in the final stage. A new study of the occurrence of CK-BB in small cell carcinoma of the lung and its role in diagnosis and response to therapy is in advanced stages. CK-BB seems to be a good marker in separating small cell carcinoma from other lung cancer.

A major study of a large group of patients admitted to the coronary care unit (CCU) with the suspicion of myocardial infarction was completed indicating that CK-BB is a very early and sensitive indicator of myocardial insult. These encouraging results have led to the initiation of a more comprehensive study to determine the optimum way to use this test in the diagnosis of MI.

Lithium iodoacetates has been proposed as an effective antiglycolytic agent that does not interfere with determination of other analytes. In a comparison study of serum harvested from tubes with and without lithium iodoacetate, the results show that this agent caused a significant increase in the concentration of potassium, chloride, and lactate dehydrogenase and a decrease in sodium concentration. A decision was made not to employe this as an antiglycolytic agent.

A test of the effect of bromine in blood specimens on the determination of chloride by the SMAC and the PVA-4 was performed. The results show that bromide significantly elevated chloride determinations on the PVA-4 but did not interfere with chloride values on the SMAC.

Phosphorus determinations performed on the SMAC have been consistently low when compared with other instruments and methodologies in the College of American Pathologists Proficiency Testing Program. This problem was studied by determining phosphorus in serum and performing recovery studies using the SMAC, an AutoAnalyzer method, and the classical Fiske-SubbaRow method. The results showed approximately 100% recovery using the AutoAnalyzer System and the Fiske-SubbaRow method.

The recovery of approximately 90% of added phosphorus was achieved with the SMAC. In addition, random serum specimens analyzed by the three systems showed significantly lower values on the SMAC when compared with the other two systems.

Hematology Service. Evaluation of radioimmunoassay kits for determination of platelet factor IV and beta thromboglobulin is in progress. The ability to accurately measure these products of platelet activation will be useful in the evaluation of *in vivo* platelet studies and possibly in the detection of pre-thrombotic or thrombotic states.

An assay for fibrinopeptide A is being developed in the laboratory in the hope of having a sensitive and specific indicator to investigate *in vivo* the end products of thrombin cleavage of fibrinogen by the release of fibrinopeptide A.

Investigation of the interaction of purified factors IX and VIII continued, and results indicate that factor IXa enhances and subsequently inactivates factor VIII activity in a similar manner as thrombin; however, the exact mechanism of the thrombin of factor IXa activation of factor VIII has not been completely worked out.

The study utilizing vitamin E to treat G6PD-deficient Mediterranean individuals was completed with a one-year followup. The study revealed that hemolysis was improved by vitamin E. However, studies of vitamin E therapy in G6PD deficient patients with chronic hemolysis revealed no improvement in hemolysis. A second study has been undertaken with a more potent antioxidant to try to correct the hemolytic abnormality in these patients.

The study of cold insoluble globulin (CIG) has proceeded with investigation of the interaction of CIG with various coagulation proteins. Data indicate that there is no interaction between the cold insoluble globulin and the anticoagulant portion of factor VIII. Other studies involving CIG have looked at the ability of platelets to adhere to collagen in the presence or absence of cold insoluble globulin.

Studies have been undertaken on the carbohydrate content of coagulation proteins in neoplasia. In particular, the carbohydrate content of fibrinogen and the possibility of interference or interaction of these carbohydrates in fibrinogen function *in vivo* and *in vitro*.

A thorough investigation of variables involved in the prothrombin time has been undertaken. These include the nature and type of anticoagulant, the surface of the container in which the blood is collected, the temperature at which it is stored, the time for which it is stored, the container in which the plasma is stored, and the time of plasma storage. These studies have been useful in indicating areas in which the samples of coagulation testing are prone to artifactual changes which will significantly alter the results. Further studies are underway in an attempt to reduce the artifactual changes.

Studies of the French, American and British Group have continued with a new classification for acute lymphocytic leukemia. This new classification is a more reproducible form and should prove to be useful in looking at prognostic features in childhood and adult lymphocytic leukemia.

Studies of patients with inhibitors of blood coagulation have indicated a variety of different sites of inhibition, one being a heparin-like anticoagulant and another being an antiprothrombinase anticoagulant. Biochemical characterization of these inhibitors is currently underway.

A clinical study of von Willebrand factor variants with coagulation and immunologic studies is in progress. This study will attempt to correlate all of the immunologic and coagulation abnormalities in patients with von Willebrand's disease in order to increase our understanding of this disorder.

A method for the collection of units of young red blood cells (neocytes) with enhanced in vivo survival has been developed. Three patients are being supported by these red cells, and the methodology is being further refined.

Studies on the effect of factor VIII/von Willebrand factor protein and the canine cerebral ischemia model have continued with the use of autologous factor VIII/von Willebrand factor protein infused into dogs. Studies reveal that the factor VIII/von Willebrand factor protein significantly reduces circulation of blood to the brain after cerebral ischemia while blood devoid of the factor VIII/von Willebrand factor protein enhances recirculation to brain tissue.

A clinical study involving splenectomy in patients with Wiscott-Aldrich syndrome and thrombocytopenia was completed and revealed that the value of the platelet size is a predicator of response to splenectomy.

Study on the factor VIII/von Willebrand factor components of the platelet membrane indicate that the factor VIII-related antigen was present while the factor VIII coagulant antigen was absent on the surface of platelets. Inhibition of the factor VIII-related antigen on the platelet surface did not interfere with ristocetin-induced platelet aggregation.

Further investigations of the bonding of factor VIII/von Willebrand factor protein to platelets have indicated that the low molecular weight factor VIII/von Willebrand factor proteins, although able to bind significantly to the platelet surface, do not in themselves induce agglutination or aggregation of platelets. These studies have indicated that the binding of these proteins is related to the fact that they occupy low affinity binding sites rather than high affinity binding sites.

Studies of platelet survival in an animal system are in progress involving splenectomized rabbit model to look at platelet age and density as a model for platelet survival.

The Hematology Service introduced a Thrombosis Unit. This unit will develop assays for detection of platelet activation, thrombin formation, and fibrinogen conversion to fibrin by utilizing sensitive and specific radioimmunoassays. The use of this type of system will allow for preclinical detection of patients with activation of coagulation, activation of platelets, or the development of intervascular coagulation or thrombosis.

The Laboratory Computer Service is providing computer support for a prospective study of laboratory reference ranges and long term biological variation in NIH employees.

The evaluation of computerized impedance monitoring for the detection of bacterial growth in blood cultures is continuing in collaboration with the Microbiology Service.

The feasibility of using antimicrobial sensitivity measurements for the computerized identification of bacteria is being studied in cooperation with the Microbiology Service.

A study with the Clinical Chemistry Service of individuals admitted to a coronary care unit care unit is determining time-specific decision limits for a group of laboratory tests used to diagnose or exclude acute myocardial infarctions in this patient population.

The Department's *Staphylococcus aureus* phage typing database has been updated. Computer analysis of patterns of phage lysis continues.

Statistical analysis of the data obtained in the Department's nationwide survey of the resources and work loads of academically affiliated pathology departments continues.

Microbiology Service. The studies on antibiotic synergy and antimicrobial susceptibility using a laser light scattering instrument, the Differential III, have been expanded to include more antibiotics and different types of organisms. The results, although encouraging, are still not consistent enough to consider routine use of this methodology.

The Microbiology Service continues to develop and improve the existing successful technique of lysis and filtration for a new and different blood culturing technique. In addition to collecting data from clinical studies, animal studies are in progress to provide controlled experiments comparing the relative abilities of the conventional and the lysis filtration blood culture techniques to recover pathogenic microorganisms from blood.

A prototype impedance detector with a capacity of 60 blood cultures has been developed and connected to a dedicated computer in the laboratory. This represents a novel approach to detection of bacterial cultures by using a very minimum amount of human intervention. the blood has been lysed and filtered before presentation to the detector to increase bacterial yield. Thus the separate techniques of impedance detection and lysis filtration blood cultures are mated. Progress has been severely hampered because of electronic unreliability, both in the impedance detection-amplifier and in the PDP 11 computer, which has the task of storing and analyzing millivolt (impedance) input signals from the 60 blood culture electrode bottles. The problems with the detector have been successfully resolved, but the PDP 11 presents continuing difficulty because of its unreliability. It is hoped that this unreliability can be corrected with more aggressive maintenance.

Study of Blastocystis-hominis, newly designated protozoan parasite of man, is continuing. By Feulgen staining, many nuclei have been characterized in single cells. By thick and thin progressive sectioning for transmission electron microscopy, we are characterizing all of the nuclei in a series of single cells to determine their places in the cell and position vis-a-vis other organelles.

Several methods of assaying gentamicin in serum have been compared, including radioimmunoassay, fluorometric immunoassay, enzyme immunoassay, bioassay, and latex agglutination inhibition. The results of this comparative evaluation will be published. On the basis of this study, the enzyme immunoassay procedure was selected as the new gentamicin assay procedure for use in our laboratory.

A study was undertaken of the feasibility of in-house preparation of plates for the identification of certain types of clinically significant Gram negative rods. While preliminary analysis suggested that such a system would be feasible, the commercial development of similar systems rendered further work in this area unjustifiable.

## C. Training

Three first year residents entered the Clinical Pathology Department residency training program. They joined four second year residents in the program. Each rotation of the first year residency training program was evaluated by the residents using an evaluation sheet developed by the Office of the Chief. All comments and evaluations were transmitted to the Chiefs of the Services. The comments indicate that all services are providing an excellent residency training program.

The senior staff and the residents continued weekly Clinical Pathology rounds in which interesting patients, laboratory problems, and original research were presented and discussed. These rounds are approved by the American Medical Association for Category 1 Continuing Medical Education credit.

Clinical Chemistry Service. The weekly lecture series given by the senior staff for continuing education of medical technologists continued. This series was approved for PACE credit. A weekly Journal Club for the senior staff members and supervisory technologists of the Chemistry Service was begun this year. It was the unanimous opinion that this was an effective way of disseminating new information in the area of clinical chemistry and it will be continued in the future.

Several members of the Hematology Service have participated in the review courses for Medicine Hematology Board Review and the Pediatric Hemato-Oncology course. Lectures have been given concerning morphology, coagulation, and general areas of hematologic malignancies.

The Hematology Service continued to coordinate the Hematology-Oncology Clinical Elective and has continued its major role in the direction and teaching of this elective. Twelve medical students took their rotations in the Hematology Service from September 1979 through May 1980. Each student had a senior staff advisor who supervised all consultations by these students and who insured that they were able to perform bone marrow aspirations and biopsies, and also assisted them in interpretation of peripheral blood smears and bone marrow material. In addition, these students participated in all conferences by presenting cases and joining in the ensuing discussions.

The rounds of the Hematology Service and Molecular Hematology Branch (NHLBI) were used by the Clinical Elective students to develop the ability to present cases and speak properly in front of a medical group. These conferences with the Molecular Hematology Branch were a success with a variety of patients being discussed and with the attendance of these conferences increasing 10% over last year.

The senior staff, residents, and medical students of the Hematology Service met at least twice weekly to have rounds related to to patients with hematologic problems. Patient care and laboratory problems were presented at these rounds and discussed. In addition, several guest physicians from other Institutes as well as some from outside the NIH attended these rounds on a regular basis.

The Hematology Service continued to give rounds once a week to the clinical associates of the National Cancer Institute on the morphology of hematologic malignant diseases involving bone marrow. This was done primarily through a morphology oriented presentation of patients and an examination of their morphologic material.

A series of continuing education topics in Special Hematology was presented to the Hematology Service technologists. This allowed the technologists to have a greater awareness of the techniques involved in some of the tests, the interpretation of the laboratory data, and the application of these data to patient problems.

The Laboratory Computer Service conducted training in medical computing and the use of NIH computer systems for resident physicians of the Clinical Pathology Department. In addition, personnel from other Services were instructed and assisted in the use of the NIH computer facilities.

Microbiology. A second year resident in Clinical Pathology has started a year's rotation in the Service.

The senior staff gave weekly lectures on practical bacteriology to the Clinical Pathology residents.

Two courses, one in enteric pathogens and the other in mycology, were approved for PACE credit for the medical technologists and microbiologists. Approximately 20 individuals completed each course.

Weekly conferences at which interesting cases were discussed with the senior staff and technologists were continued.

## IV. FUTURE OBJECTIVES

The Office of the Chief now has in place a superior management tool to evaluate deficient utilization of personnel, i.e. the College of American Pathologists Workload System. This system will be used for the allocation of personnel resources within the Department and will enable a comparison of this Department with other Clinical Pathology Departments in the country. The Office of the Chief will attempt to carefully evaluate the purchase of equipment for the Department, attempting to balance the quality of service with reasonable fiscal goals.

The Office of the Chief has the responsibility for coordinating the move of the Department to the new facilities in the Ambulatory Care Research Facility. Every attempt will be made to minimize any disruption in the services offered by the Department.

The Phlebotomy and Urine Collection Service will attempt to extend the hours of service beyond 5:00 p.m. and to offer limited service on weekends. This extension of the service will be contingent upon additional personnel resources.

The Clinical Chemistry Service will maintain the highest standards of quality while simultaneously increasing efficiency and output, as well as expanding the services offered to Clinical Center patient care personnel. Through research and development and the use of new technology as it enters the market place, we hope to increase the accuracy and specificity of our tests and to investigate the clinical applicability of new areas of testing.

The major future objective of the Chemistry Service is to perform essentially all analyses now done via contract within the Service. The tests that will be developed during the next year have been identified (urinary cortisol, CEA, insulin, growth hormone, digoxin, tegretol, 17 ketosteroids, VMA, and heavy metals) and, we hope personnel resources will permit their implementation when the Department moves into the Ambulatory Research Care Facility.

The Hematology Service plans to complete necessary steps for introducing the Thrombosis Unit into the Hematology Service. In doing so, it will allow the Clinical Center to study patients with a variety of vascular, coagulation, and thrombotic diseases. In addition, this will be the only medical center within over a 100-mile radius able to perform these tests.

During the coming year the Hematology Service will evaluate automated differential counters and automated coagulation systems in an attempt to more fully automate the Hematology Service laboratories and to allow for greater freedom of technologists to do more sophisticated testing.

The Hematology Service will continue to play an important role in the training of individuals in clinical and laboratory hematology, and will hope to improve the present standard of training. In doing so, the Hematology Service will attempt to attract individuals who have had previous pathology or internal medicine training and who are interested in intensive postgraduate training in clinical hematology, laboratory hematology, and investigative research.

Microbiology Service. New commercially available kits which contain both biochemical and antimicrobial susceptibility reagents and which can be automatically read will be evaluated. If this methodology performs to expectation, it may be possible to combine both of these processes in a much more time saving and accurate way.

The progress made in the development of lysis and filtration methods for blood cultures and the solution of certain electron problems for the detection of bacteria by measuring electrical impedence of growing cultures may permit more routine use of this promising detection method.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CC 10001-06 CP |

PERIOD COVERED
October 1, 1979 to September 30, 1980

TITLE OF PROJECT (80 characters or less)
Analytical Methodology: Development and Interpretation Application

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | |
|---|---|---|
| PI: | R. J. Elin, Chief, Clinical Chemistry Service | CP CC |
| OTHERS: | E. A. Robertson, Assistant Chief, Laboratory Computer Serv. | CP CC |
| | M. H. Zweig, Asst. Chief, Clinical Chemistry Service | CP CC |
| | Sharon McClean, Chemist | CP CC |

COOPERATING UNITS (if any)

LAB/BRANCH
Clinical Pathology Department

SECTION
Clinical Chemistry Service

INSTITUTE AND LOCATION
Clinical Center, NIH, Bethesda, Maryland

| | | |
|---|---|---|
| TOTAL MANYEARS: 8.5 | PROFESSIONAL: 3.5 | OTHER: 5 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Analytical methods in use in clinical laboratories have been evaluated. New methods and instrumentation have been studied and effects of drugs on test values determined. Continued work with automatic interpretation of effects of drugs has shown that is possible to assist physicians in understanding influence of drug therapy in changing laboratory test values.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10001-06 CP
1. Clinical Pathology Department
2. Clinical Chemistry Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 to September 30, 1980

Project Title: Analytical Methodology: Development and Interpretative Application

Previous Serial Number: Z01-CL-10001-05-CP

Principal Investigator: Ronald J. Elin

Other Investigators:
E. Arthur Robertson
Mark H. Zweig
Sharon McClean

Man Years:

| | |
|---|---|
| Total | 8.5 |
| Professional | 3.5 |
| Other | 5 |

## Project Description

Objectives

1. To upgrade the quality of clinical laboratory data within NIH and elsewhere.

2. To facilitate the correct interpretation of laboratory data.

Methods employed:

1. Reference methods have been developed against which other methods can be compared. These methods are well characterized with respect to accuracy, precision, sensitivity and specificity.

2. Data bases have been developed in files to list effects of drugs on laboratory tests, conversion factors from traditional to SI units, and centers where unusual clinical laboratory tests are performed throughout the country.

Major findings:

Deficiencies in analytical methods have been identified and alternative methods studied in depth. By appropriate selection of method it is possible to avoid erroneous answers due to nonspecificity of the procedures. Drugs have been added to serum to their therapeutic concentration and effects observed on many different procedures on several different analyzers.

Significance:

This work has upgraded the quality of some tests in this laboratory and has the potential for doing the same thing in other laboratories when the same methods are used. By alerting physicians to drugs as a possible cause of abnormal data it has been possible to explain the cause of the unusual values and to prevent extensive and unnecessary workups of patients.

Proposed course:

Continued development and evaluation of methods will be undertaken.

Publications:

Forman, D.T. and Young, D.S.: Drug interference in laboratory testing. An. Clin, Lab. Sci. 6, 263-271, 1976.

Forman, D.T. and Young, D.S.: Drug interference in laboratory testing in Clinical Chemistry, Forman, D. R. and Mattoon, R. W. eds. American Chemical Society, Washington, D. C. pp 271-284, 1976.

Hande, K. R., Perini, F., Putterman, G. and Elin, R. J.: Interference with serum uric acid determinations due to hyperxanthinemia following treatment of Burkitt's lymphoma. Clin. Chem. 25, 1492-1494, 1979.

Jaffe, R. M.: A test for occult blood. US patent serial no. 498-109.

Jaffe, R., Schmid, A. and MacLowry, J.: Effect of ascorbic acid on detection of blood in urine. Am. J. Clin. Path. Sept. 1979.

McClean, S. W., Young, D. S. and Yonekawa, W. : Anticonvulsants in serum, determined with a fully mechanized enzyme analyzer. Clin. Chem. 23, 116-118, 1977.

McClean, S. W., Elin, R. J., Alling, D., Chesler, R., Siegel, S., Utter, A. R., and Green, M.: Comparison of four electrolyte instruments using the proposed NCCLS protocol for evaluation of precision and accuracy of automated instruments. Clin. Biochem. In Press.

Robertson, E. A., Sliva, C. A. and Young, D. S.: Values for uric acid in patients' sera as measured with SMAC (phosphotungstate) and AutoAnalyzer (uricase). Clin. Chem. 24, 173, 1978.

Robertson, E. A. and Young, D. C.: Evaluation of SMAC performance by analysis of variance of quality control data. Advances in Automated Analysis, Vol. 1, Tarrytown, N. Y.: Mediad, Inc., pages 204-210, 1977.

Rodbard, D. and McClean, S. W. : Automated computer analysis for enzýme-multiplied immunological techniques. Clin. Chem. 23, 112-115, 1977.

Young, D. S. and Panke, E.: Effects of drugs on the analytical procedure of a multitest analyzer. In Siest, G., and Young, D. S. (eds.): Drug Interference and Drug Measurement in Clinical Chemistry. Karger, Basel, pp 10-20, 1976.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NOTICE OF
INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01-CL-10004-05 CP

PERIOD COVERED
October 1, 1979 to September 30, 1980

TITLE OF PROJECT (80 characters or less)

Radioimmunoassay of creatine kinase isoenzymes

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Dr. Mark H. Zweig, Staff Physician and Asst. Chief, Clinical Chemistry Service, CP, CC

Dr. Sharon McClean, Chemist, CP, CC

COOPERATING UNITS (if any) Dr. Andre Van Steirteghem, Burssels, Belgium; Dr. Ronald Feld, Univ. of Iowa; Dr. Lawrence Silverman, NC Memorial Hospital, Chapel Hill; Dr. Adi Gazdar and Dr. Daniel Ihde, NCI Oncology, VA Hospital, Washington, D.C.

LAB/BRANCH
Clinical Pathology Department

SECTION
Clinical Chemistry

INSTITUTE AND LOCATION
CC, NIH, Bethesda

| | | |
|---|---|---|
| TOTAL MANYEARS:<br>1.5 | PROFESSIONAL:<br>0.5 | OTHER:<br>1.0 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Previously we developed a specific radioimmunoassay for the BB isoenzyme of creatine kinase (CK-BB). Currently, we are applying this assay to the measurement of CK-BB in human serum and other body fluids, human tumor homogenates, and cell cultures. Serum levels of CK-BB are an early and sensitive marker of acute myocardial infarction. Since serum levels of CK-BB are also elevated in the presence of a number of cancers, we have investigated the role of CK-BB as a tumor marker in patients with cancer of the lung, gastrointestinal and genitourinary tracts. It appears that CK-BB may be most useful in patients with small cell carcinoma of the lung.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10004-05 CP
1. Clinical Pathology Department
2. Clinical Chemistry Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Radioimmunoassay of Creatine Kinase Isoenzymes

Previous Serial No.: Z01 CL 10004-04

Principal Investigator: Dr. Mark Zweig

Other Investigator: Dr. Sharon McClean

Cooperating Units: Dr. Andre Van Steirteghem, Vrije Universiteit, Brussels, Belgium; Dr. Ronald Feld, Department of Pathology, University of Iowa; Dr. Lawrence Silverman, NC Memorial Hospital, Chapel Hill; Drs. Adi Gazdar and Daniel Ihde, NCI Oncology Branch, VA Hospital, Washington, D.C.

Man Years:
Total 1.5
Professional 0.5
Other 1.0

# Project Description

## Objectives:

1. To apply a previously developed RIA for creatine kinase isoenzyme BB (CK-BB) to the diagnosis and study of disease of tissues and organs containing CK.

2. To optimize and shorten the assay for CK-BB so that it is more practical for routine clinical laboratory use and so that more research assays can be performed in a given time.

## Methods Employed:

1. Serum and pleural fluid were obtained from patients with a variety of benign and malignant disorders.

2. Lung tumor cell homogenates, lung tumor tissue culture homogenates and supernatant fluids were obtained.

3. CK-BB by RIA was determined on all specimens.

4. Prostatic acid phosphatase by commercial RIA kits was determined on specimens from patients with urogenital disease.

5. Total CK and CK isoenzymes by electrophoresis were assayed in tumor cell homogenates, cell culture homogenates and supernatants.

6. Patient serum with a variety of CK-BB levels were assayed by both short and regular CK-BB assay to validate the new shorter assay.

## Major Findings:

CK-BB concentration in serum is elevated in patients with a variety of malignancies but usually with low frequency. In the case of prostatic cancer, prostatic acid phosphatase is elevated much more frequently than CK-BB. However, CK-BB appears to be associated with small cell carcinoma of the lung, in those cases where the disease is extensive. In gastrointestinal cancers, CK-BB may be useful if used together with CEA.

CK-BB was found to be an early and sensitive indicator of acute myocardial infarction, usually becoming abnormal before CK-MB by immunoinhibition.

By changing reagent concentrations and incubation conditions a 4.5 hour shortened assay was developed which performs similarly to the original long assay. More assays can be done per week and results are available much faster.

## Significance to Biomedical Research and the Program of the Institute:

The evidence thus far collected suggests that the determination of CK-BB by RIA will ultimately have a role in the routine clinical laboratory diagnosis of myocardial infarction, and in the diagnosis and follow-up of certain patients with cancer. Studies such as we are doing are necessary first in order to determine the diagnostic use of the test and the most efficient application.

## Proposed Course:

Studies of CK-BB in myocardial infarction will continue, in order to compare CK-BB to other conventional markers and to define more precisely how best to use CK-BB in patient management. Two studies of CK-BB in prostatic cancer are still underway and will continue into the next fiscal year. Our work on the role of CK-BB in the evaluation and management of patients with small cell carcinoma of the lung will continue.

## Publications:

1. Silverman, L.M., Dermer, G.B., Zweig, M.H., Van Steirteghem, A.C., and Tokes, Z.A. Creatine kinase BB: A new tumor-associated marker. Clin. Chem. 25, 1432-1435 (1979).

2. Zweig, M.H., Adornato, B., Van Steirteghem, A.C. and Engel, W.K.; Serum creatine kinase BB and MM concentrations determined by radioimmunoassay in neuromuscular disorders. Ann. Neurol. 7, 324-328 (1980).

3. Feld, R.D., Van Steirteghem, A.C., Zweig, M.H., Weimar, G.W., Narayana, A.S., and Witte, D.L.: The presence of creatine kinase BB isoenzyme in patients with prostatic cancer, Clin. Chim. Acta, 100, 267-273 (1980).

4. Van Steirteghem, A.C., Zweig, M.H., Bernard, R.M., Putzeys, G.A., and Bieva, C.J.: Creatine kinase isoenzyme BB concentration in serum as a marker of myocardial infarction. Clin. Chem. 26, 1110 (1980).

| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01-CL-10005-06 CP |
|---|---|---|

PERIOD COVERED

October 1, 1979 to September 30, 1980

TITLE OF PROJECT (80 characters or less)

Development of a Nephelometric Procedure for the Quantitation of Pyrogens

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

H. Harold Nishi, CC, CPD - Research Biochemist, Principal Investigator

Ronald J. Elin, M.D.

COOPERATING UNITS (if any)

None

LAB/BRANCH

Clinical Pathology Department

SECTION

Clinical Chemistry Service

INSTITUTE AND LOCATION

Clinical Center, NIH, Bethesda, MD 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.30 | .30 | 1.0 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Endotoxins of gram-negative bacteria were found to react with the lysate of L. polyphemus amebocytes to form fine precipitin-like particles in the presence of large quantities of pyrogen-free sterile water. Light scatter measurements during the formation of these particles indicated that the rate of formation to be a function of endotoxin concentration. A nephelometric procedure for the quantitation of pyrogens (endotoxins of gram-negative bacteria) with Limulus amebocyte lysate (LAL) was developed and optimized by studying the various parameters of the reaction. The finalized procedure was established as 200 µl of LAL reagent with 100 µl of an endotoxin solution (reference or unknown solution) diluted to 2 ml with pyrogen-free sterile water. The end-point of the analysis was chosen as that time (minutes) at which the light scattering capacity of the particles reached 10 light scatter units above its baseline value. Studies indicated that the end-point data obtained on different levels of endotoxin can be defined with a mathematical formula. The standard curve data plotted on semi-log graph paper was a straight line. Reproducibility studies showed that the method was capable of giving a precision of 13% when testing endotoxin at a level of 100 pg/ml. The procedure permitted the quantitation of endotoxin as low as 16 pg/ml.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10005-06 CP
1. Clinical Center, Clinical Pathology
   Department
2. Clinical Chemistry Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Previous Serial Number: Z01 CL 10005-05 CP

Principal Investigator: H. Harold Nishi

Other Investigator: Ronald J. Elin, M.D.

Cooperating Units: Inside NIH

Man Years:

| | |
|---|---|
| Total: | 1.30 |
| Professional | .30 |
| Other | 1.0 |

## Project Description

### Objective

The object of this research project is to develop a sensitive assay procedure for the quantitation of pyrogens (endotoxins of gram-negative bacteria) using the lysate of amebocytes from *Limulus polyphemus*.

### Method Employed

Nephelometry is used to measure the rate of precipitin-like particle formation resulting from the reaction of specific protein(s) found in the lysate of *Limulus polyphemus* amebocytes with endotoxins from gram-negative bacteria.

### Major Findings

The formation of light scattering precipitin-like particles during the reaction between pyrogens (endotoxins of gram-negative bacteria) and lysate of amebocytes from *Limulus polyphemus* (limulus amebocytes lysate--LAL) in large quantities of water indicated a possible quantitation of endotoxins by nephelometry. Light scatter measurements indicated that the rate of formation of these particles to be a function of endotoxin concentration. On the basis of these findings a new nephelometric procedure for the assay of endotoxins was formulated. The new procedure requires 200 1 of LAL reagent with 100 1 of an endotoxin solution or a dilution thereof (reference or unknown sample), in 2 ml with pyrogen-free sterile water. The end-point of the analysis was chosen at that time at which the light scattering capacity of the particles reach 10 light scatter units (LSU) above its baseline value.

## Major Findings (continued)

The rate of reaction or the increase in light scatter of the endotoxin and the reagent was found to follow a mathematical model of Log Y=mX + a. The Y is the concentration of endotoxin in the sample in pg/ml, X is the time in minutes when 10 LSU was reached, m is the slope, and a is the Y intercept. The new procedure was optimized by studying the various parameters of the reaction and tested for reproducibility. Our present procedure indicates that endotoxins in fluids can be quantitated in the range of 16 to 1000 pg/ml with a precision of 13 and 11% at 100 and 500 pg/ml, respectively.

## Significance

Based on the aggregate of our experience and the knowledge gained from our studies, we have developed a nephelometric assay procedure for endotoxins using lysate of L. polyphemus amebocytes which provides a simple reliable system for the quantitation of endotoxin for diagnostic care of NIH patients.

## Proposed Course

1. To publish paper describing the new nephelometric procedure - in progress.
2. To automate the nephelometric procedure for endotoxin quantitation.
3. To increase rate of analyses by using kinetic rate measurements of endotoxin and LAL reaction.

## Honors and Awards

None

## Publications

None

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL-10006-04 CP |

PERIOD COVERED
October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Use of Laser Light Scattering for Rapid Determination of Potential Antibiotic Susceptibility and Synergy

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: Dr. James D. MacLowry, Chief, Microbiology Service, CPD, CC

COOPERATING UNITS (if any)

LAB/BRANCH
Clinical Pathology Department

SECTION
Microbiology Service, Laboratory Computer Service

INSTITUTE AND LOCATION

| | | |
|---|---|---|
| TOTAL MANYEARS: 1.1 | PROFESSIONAL: 0.1 | OTHER: 1.0 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The Differential III laser light scattering instrument is being evaluated for its potential usefulness for rapidly determining antibiotic synergy as well as antimicrobial susceptibility.

Project No. Z01-CL-10006-04 CP
1. Clinical Pathology Department
2. Microbiology Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Use of Laser Light Scattering for Rapid Determination of Potential Antibiotic Susceptibility and Synergy

Previous Serial No.: Z01-CL-10006-03

Principal Investigator: Dr. James D. MacLowry
Other Investigator: None
Cooperating Units: None

Man Years: Total 1.1
Professional 0.1
Other 1.0

## Project Description

### Objectives:

Evaluation of a prototype light scattering instrument, the Differential III for its potential use in clinical microbiology.

### Methods Employed:

Antibiotic combinations are being evaluated with a novel laser light scattering instrument to detect changes in bacterial growth. The output of this instrument is captured on computer disc for mathematical evaluation.

### Major Findings:

The laser light scattering technique is very sensitive to the presence of and shape of particles. A variety of Group D streptococci have been tested with varying combinations of penicillin and aminoglycoside antibiotics. A number of different media have been used in an attempt to derive consistent results. Thus far some strains can be predicted to evidence synergistic killing with some antibiotic combinations, but inconsistency in results has not been overcome.

## Proposed Course:

Evaluation will continue until instrument has been adequately evaluated.

## Honors and Awards:

None

## Publications:

None

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-10009-05 CP |

PERIOD COVERED
October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Blastocystis hominis, Structure, and Physiology (continued study)

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: Dr. Charles H. Zierdt, Microbiologist, Microbiology Service, CPD, CC

COOPERATING UNITS (if any)

None

LAB/BRANCH
Clinical Pathology Department

SECTION
Microbiology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.1 | 0.25 | 0.75 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Blastocystis hominis, a protozoan parasite of the human gastrointestinal tract and an organism implicated in the causation of human diarrhea, is being studied in terms of its morphology, physiology, and sensitivity to metronidazole, enterovioform and similar drugs. This sporozoan may contain hundreds of mitochondria, although it is a strict anaerobe. Whether these are anaerobic mitochondria, and their enzyme activity, if any, are subjects of the study.

Mean generation time of B. hominis is from 5-10 hours.

B. hominis is sensitive to metronidazole, enterovioform, and other oxyquinoline derivatives.

Cell division of B. hominis is commonly asexual, with sexual reproduction occurring rarely.

PHS-6040
(Rev. 10-76)

Project No.: Z01-CL-10009-05 CP
1. Clinical Pathology Dept.
2. Microbiology Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Blastocystis hominis, Structure, and Physiology (Cont'd study)

Previous Serial No.: Z01-CL-10009-04 CP

Principal Investigator: Dr. Charles H. Zierdt

Man Years:
Total: 1.0
Professional 0.25
Other: 0.75

## Project Description

### Objectives:

Continuing study of Blastocystis hominis, newly designated protozoan parasite of man. By Feulgen staining many nuclei have been characterized in single cells. By thick and thin progressive sectioning for transmission electron microscopy, we are characterizing all of the nuclei in a series of single cells, to determine their places in the cell, and position vis a vis other organelles.

### Methods Employed:

Study of diarrhea caused by B. hominis, and the ultrastructure, physiology and life cycle of this organism. New culture methods, cell division time (generation times) and sensitivity studies (to appropriate drugs).

### Major Findings:

1. This protozoan intestinal parasite of man is a strict anaerobe, that dynamically self-destructs on exposure to air, yet includes in some cells, hundreds of mitachondria. These may be non-functional, vestigial organelles, or they might be an example of anaerobic mitachondria. Enzyme studies to date indicate that the latter may be so.

2. Mean generation time for B. hominis strains is from 5 to 10 hours.

3. There is increasing interest in B. hominis as a cause of diarrhea in man. In this laboratory, when large numbers of B. hominis are seen in a fecal sample, the patient has diarrhea.

4. The ultrastructure of B. hominis has now been well described. Division is commonly asexual, but sexual reproduction also occurs. Nuclear division with formation of new cell membranes may result in "cells within a cell", a phenomenon also seen with *Pneumocystis carinii* in human lung.

5. Drug sensitivity testing has shown that oxyquinolin derivatives are effective against *B. hominis*. Metronidazole is very effective, as is enterovioform. Other drugs are currently being tested.

Publications:

Phillips, B.P. and Zierdt, C.H.: *Blastocystis hominis*: Pathogenic Potential in Human Patients and in Gnotobiotes. *Experimental Parasitology*. 39: 358-364, 1976.

Zierdt, C.H. and Tan, H.K.: Ultrastructure and Light Microscope Appearance of *Blastocystis hominis* in a Patient with Enteric Disease. Z. Parasitenk. 50: 277-283, 1976.

Zierdt, C.H.: *Blastocystis hominis*, an intestinal protozoan parasite of man. The Public Health Lab. 36: 147-159, 1978.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CC 10010-05 CP |

PERIOD COVERED
October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Effect of Magnesium Deficiency on Erythrocyte Structure and Function

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Dr. Ronald J. Elin | Chief, Clin. Path. Dept. | CP CC |
| OTHER: | Dr. Laurence Corash, | Asst. Chief, Hematology Serv. | CP CC |

COOPERATING UNITS (if any)

None

LAB/BRANCH
Clinical Pathology Department

SECTION
Hematology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2 | .05 | 1 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Magnesium deficiency in experimental animals produces an anemia and a shortened erythrocyte survival. Experimental animals with severe magnesium deficiency produce erythrocytes with normal magnesium content, enzyme concentrations and structure. However, once this erythrocyte is subjected to an environment deficient in magesium (plasma) structural and biochemical abnormalities occur which lead to the shortened erythrocyte survival.

PHS-6040
(Rev. 10-76)

Project No. Z01 CC 10010-05 CP
1. Clinical Pathology Dept.
2. Hematology Service
3. Bethesda, Maryland

PHS-NIH

Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Effect of Magnesium Deficiency on Erythrocyte Structure and Function

Previous Serial Number: Z01 CL 10010-04 CP

Principal Investigator: Dr. Ronald J. Elin
Other Investigator: Dr. Laurence Corash

Man Years:
Total: 2
Professional: .05
Other: 1.0

## Project Description

### Objectives:

Define and characterize membrane abnormalities associated with deficiency of magensium. Determine the effect of magnesium deficiency on erythropoiesis.

### Methods Employed:

The erythrocyte specimen was prepared by freeze-fracture and etching. The etched surface was coated with carbon and platinum. The specimen was then studied using an electron microscope. Erythrocytes from magnesium-deficient rats were separated on the basis of age using a stractan gradient. The magnesium concentration and pyrophosphatase activity were determined for each population of erythrocytes using standard techniques.

### Major Findings:

The erythrocytes from magnesium-deficient rats develop membrane alterations in the form of a plaque. These plaques were present on erythrocyte ghosts prepared by osmotic lysis. The membrane plaques were unaltered by incubating the cells in normal concentrations of magnesium. Erythropoiesis in magnesium-deficient rats is normal since reticulocytes and very young erythrocytes have a normal magnesium content, and normal concentration of erythrocyte pyrophosphatase and have a normal membrane surface. More mature erythrocytes show a decreased magnesium content, decreased erythrocyte pyrophosphatase activity and the development of membrane abnormalities in the form of plaques. In addition, the examination of the bone marrow of these animals shows normal erythroid precursors and an increased myeloid component.

Significance to Biomedical Research and the Program of the Department:

This is the first membrane abnormality of erythrocytes in experimental animals that is related to an abnormality in mineral metabolism. Magnesium has been clearly established as an essential element for biochemical processes involving energy production. In this study, magnesium has been shown to be important for normal membrane structures. This is part of a series of studies by the Department to define factors which influence erythrocyte survival and function. The structural and biochemical abnormalities of erythrocytes in magnesium deficiency occur after the cell has entered the vascular space. Thus, the bone marrow is able to produce a normal cell but an environment deficient in magnesium produces erythrocyte abnormalities.

Proposed course:

This project will now be extended to study factors of erythropoiesis that enable the synthesis of a relatively normal cell in magnesium deficiency and to assess the biochemical abnormality in the cell membrane of erythrocytes from magnesium deficient animals.

Honors and Awards: None

Publications:

Elin, R. J.: Erythrocyte survival in magnesium-deficient rats. Proc. Soc. Exp. Biol. Med. 142: 1159-1161, April 1973.

Elin, R. J.: The effect of magnesium deficiency in mice on serum immunoglobulin concentrations and antibody plaque-forming cells. Proc. Soc. Exp. Biol. Med. 148: 620-624, March 1975.

Elin, R. J., and Tan, H. K.: Erythrocyte membrane plaques from rats with magnesium deficiency. Blood. 49:657-663, April 1977.

Elin, R. J. and Alling, D. W.: Survival of normal and magnesium-deficient erythrocytes in rats: effect of magnesium-deficient diet vs. splenectomy. J. Lab. Clin. Med., 91: 666-672, 1978.

Elin, R. J. and Tan, H. K.: Formation of plaques on erythrocyte membranes from rats with magnesium deficiency. Blood. 49: 657, 1977.

Elin, R. J.: Role of magnesium in membranes; erythrocyte and platelet function and stability. In Cantin, M. (ed.): Proceedings of the Second International Symposium on Magnesium. Spectrum Publications, New York. 1980.

Elin, R. J. and Tan, H. K.: Formation of plaques on erythrocyte membranes from rats with magnesium deficiency. In Cantin, M. (ed.): Proceedings of the Second International Symposium on Magnesium. Spectrum Publications, New York. 1980.

Publications: (Continued)

Elin, R. J., Utter, A., Tan, H. K., and Corash, L.: Effect of magnesium deficiency on erythrocyte aging in rats. Am. J. of Pathol. In Press.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 10012-12 CP |

PERIOD COVERED
October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Investigation of Hemorrhagic and Thrombotic Disorders in Man

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: Dr. Harvey R. Gralnick — Chief, Hematology Service, CPD, CC

COOPERATING UNITS (if any)

LAB/BRANCH
Clinical Pathology Department

SECTION
Hematology Service

INSTITUTE AND LOCATION
Clinical Center, NIH, Bethesda, MD 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 11.0 | 5.5 | 5.5 |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☒ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Investigation of congenital and acquired hemorrhagic and thrombotic disorders in man to elucidate the clinical entities and to investigate the molecular basis for the defects. This has involved purification of coagulation proteins, immunologic investigation of coagulation proteins and inhibitors, and defining the role of these proteins in normal hemostasis and abnormal hemostasis.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10012-12 CP

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Investigation of Hemorrhagic and Thrombotic Disorders in Man

Previous Project Number: Z01 CL 10012-11 CP

Principal Investigator: Dr. Harvey R. Gralnick

Man Years:

| | |
|---|---|
| Total: | 11.0 |
| Professional: | 5.5 |
| Other: | 5.5 |

## Project Description

### Objectives:

Define and characterize normal and abnormal coagulation proteins, inhibitors, and cofactors associated with clinical disorders of hemostasis.

### Methods Employed:

Purification and isolation of various coagulation proteins, determination of functional defects, and molecular characterization of the defect. In addition, multiple immunologic techniques are utilized for elucidation of abnormal proteins.

### Major Findings:

Three families with congenital dysfibrinogenemia have been fully described and elucidated. These families have defects in the conversion of fibrinogen to fibrin which interferes with normal hemostasis in two of the three families. The abnormalities vary in each family and in some families have been related to the release of fibrinopeptides and in others to polymerization of fibrin monomers. Studies of the pathological aspects of fibrinogen have indicated the importance of fibrinogen in maintenance of normal hemostasis. In particular, defects were observed in immunologic techniques, clotting techniques, and in the ability of fibrinogen to cross-link. In one family, the abnormal fibrinogen also had a markedly shortened intravascular survival.

Significance to Biomedical Research and the Program of the Department:

These studies elucidate some of the molecular defects associated with abnormal hemostasis and thrombosis and have allowed a greater understanding of the pathophysiology of blood coagulation. Not only have individual patients benefited from the elucidation of these defects in proper therapy but our greater understanding of blood coagulation in general has developed. This is part of a series of studies by this service to define the factors associated with hemorrhage and thrombosis in man.

Proposed Course:

This project will be extended to study other coagulation states and thrombotic states.

Honors and Awards:

None

Publications:

1. Gralnick, H., Abrell, E., and Bagley, J.: Heparin Treatment for Hemorrhagic Diathesis of Acute Promyelocytic Leukemia. Am. J. Med. 52: 167, 1972.

2. Gralnick, H., Givelber, H., Shainoff, J., and Finlayson, J.: Fibrinogen Bethesda: A Congenital Dysfibrinogenemia with Impaired Fibrinopeptide Release. J. Clin. Invest. 50: 1819, 1971.

3. Gralnick, H. and Abrell, E.: Studies of the Proccagulant and Fibrinolytic Activity of Promyelocytes in Acute Promyelocytic Leukemia. Brit. J. Haematol. 24: 89, 1973.

4. Gralnick, H. and Finlayson, J.: Congenital Dysfibrinogenemias. Ann. Int. Med. 77: 471, 1972.

5. Gralnick, H., Marchesi, S. and Givelber, H.: Intravascular Coagulation in Acute Leukemia. Blood 40: 709, 1972.

6. Gralnick, H., Givelber, H., and Finlayson, J.: A New Congenital Abnormality of Fibrinogen: Fibrinogen Bethesda II. Thromb. Diath. Haemorrh. 29: 562, 1973.

7. Gralnick, H. and Tan, H.: Acute Promyelocytic Leukemia: A Model for Understanding the Role of the Malignant Cell in Hemostasis. Hum. Pathol. 5: 661, 1974.

8. Frantantoni, J., Pollet, R., and Gralnick, H.: Heparin-induced Thrombocytopenia: Confirmation of Diagnosis with In Vitro Methods. Blood 45: 395, 1975.

9. Gralnick, H. and Sultan, C.: Acute Promyelocytic Leukemia: Haemorrhagic Manifestation and Morphologic Criteria. Brit. J. Haematol. 29: 273, 1975.

10. Greipp, P. and Gralnick, H.: Platelet to Leukocyte Adherence Phenomena Associated with Thrombocytopenia. Blood 47: 513, 1976.

11. Hoover, Jr., H. C., Ketcham, A. S., Millar, R. C., and Gralnick, H. R.: Osteosarcoma: Improved Survival with Anticoagulation and Amputation. Cancer 41: 2475, 1978.

12. Horvath, A. and Gralnick, H. R.: The $^{125}$I Fibrinogen Euglobulin Lysis Test. Am. J. Clin. Path. 70: 271, 1978.

13. Spellman, Jr., G. G., Macoviak, J. A., and Gralnick, H. R.: Comparison of Polymerization of Ancrod and Thrombin Monomers. Blood 50: 619, 1977.

14. Gralnick, H. R.: Intravascular Coagulation. 1. Differential Diagnosis and Conditioning Mechanisms, and 2. Underlying Conditions and Therapy. Postgraduate Medicine 62: 68, 1977.

15. Gralnick, H. R., Givelber, H., and Abrams, E.: Dysfibrinogenemia Associated with Hepatoma: A Carbohydrate Abnormality. N. Engl. J. Med. 299: 221, 1978.

16. Coller, B., Chabner, B., and Gralnick, H.: Frequencies and Patterns of Bone Marrow Involvement in Non-Hodgkin's Lymphomas: Observations on the Value of Bilateral Biopsies. Am. J. Hematol. 3: 105, 1977.

17. Flaum, M., Cuneo, R., Appelbaum, F., Deisseroth, A., Engel, W. and Gralnick, H.: The Hemostatic Imbalance of Plasma-Exchange Transfusion. Blood 54: 694, 1979.

18. Bennett, J., Catovsky, D., Daniel, M.-T., Flandrin, G., Galton, D., Gralnick, H. and Sultan, C.: A Variant Form of Hypergranular Promyelocytic Leukaemia (M3). Ann. Int. Med 92: 261, 1980.

19. Smith, P., Sobotka, A., Bleecker, E., Traystman, R., Kaplan, A., Gralnick, H., Valentine, M., Permutt, S. and Lichtenstein, L.: Physiologic Manifestations of Human Analphylaxis. J. Clin. Invest. (in press).

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 10013-12 CP |

PERIOD COVERED

October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Chemical and Structural Studies on the Human Factor VIII/von Willebrand Factor Protein

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: Harvey R. Gralnick, M.D. Chief, Hematology Service, CP, CC

COOPERATING UNITS (if any)

Barry S. Coller, M.D., Div. of Hematol., School of Med., State Univ. of NY at Stony Brook, Stony Brook, NY.

Yvette Sultan, M.D., Dept. of Hematol., Hopital Saint-Louis, Paris, France

LAB/BRANCH

Clinical Pathology Department, Clinical Center

SECTION

Hematology Service

INSTITUTE AND LOCATION

Clinical Center, NIH, Bethesda, MD 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 12.0 | 6.0 | 6.0 |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☒ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The long-range purpose of this project is to initially study the immunologic aspects of the factor VIII/von Willebrand factor protein and then to study the biochemistry and structure of this protein in man. The topics of present interest are: (1) the defect of the factor VIII/von Willebrand factor protein in hemophilia A, (2) the defect of the factor VIII/von Willebrand factor protein in von Willebrand's disease, (3) the importance of carbohydrate content in biological functions, (4) the relationship of carbohydrate content to atherosclerosis, (5) the mechanism of thrombin activation, and (6) biochemical characterization of the biologically active sites of the factor VIII/von Willebrand factor protein.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10013-12 CP

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Chemical and Structural Studies on the Human Factor VIII/von Willebrand Factor Protein

Previous Serial Number: Z01 CL 10013-11 CP

Principal Investigator: Dr. Harvey R. Gralnick

Other Investigators:
Dr. Barry S. Coller
Dr. Yvette Sultan

Man Years:

| | |
|---|---|
| Total: | 12.0 |
| Professional: | 6.0 |
| Other: | 6.0 |

## Project Description

### Objectives:

Define and characterize the normal factor VIII/von Willebrand factor protein, to elucidate the defects of the protein in hemophilia and von Willebrand's disease and then to ascertain its role in atherosclerosis.

### Methods Employed:

This has been accomplished by limited alpha chymotrypsin digestion of cryoprecipitate or other concentrates of factor VIII followed by gel chromatography on Sepharose 4B.

### Major Findings:

Individuals with hemophilia A have a protein identical to normal in all respects except that it lacks clot-promoting activity while in von Willebrand's disease it has been found that the protein is quite heterogeneous. In some patients there is a complete absence of the protein with all its associated biological functions (quantitative defect) while in other patients there is a qualitative defect where the protein is present in normal amounts; however, it is deficient in biological activity. A major finding has been that the carbohydrate moiety of the factor VIII/von Willebrand factor protein is most important in its interaction with the platelets and vessel wall and may play an important role in the maintenance of normal hemostasis and propagation of atherosclerosis.

## Significance to Biomedical Research and the Program of the Department:

These studies further our long-term project of investigating hemorrhagic and thrombotic clinical disorders. The finding of the importance of carbohydrate in the interaction of platelets with vessel wall or with each other may not only be of major significance in the understanding of von Willibrand's disease but may be equally important in understanding the propagation of atherosclerosis.

## Proposed Course:

This project will be continued in its present phase with greater emphasis placed on the contribution of carbohydrates to platelet/platelet and platelet/vessel wall interaction. In addition, studies are underway to localize the sites on the factor VIII/von Willebrand factor protein which are involved in these interactions. Modification of these sites will be attempted in an effort to reproduce in vitro a von Willebrand's disease-like state.

## Honors and Awards:

1976 Fight for Sight Award for "von Willebrand Factor and Effect on Platelet Aggregation of Plasma from Diabetics with Retinopathy." Association for Research in Vision and Ophthalmology, Inc.

## Publications:

1. Gralnick, H., Abrell, E., and Bagley, J.: Immunologic Studies of Factor VIII (Antihemophiliac Globulin) in Hemophilia A. Nature 230: 9, 1971.

2. Marchesi, S., Shulman, N., and Gralnick, H.: Studies on the Purification and Characterization of Human Factor VIII. J. Clin. Invest. 51: 2151, 1972.

3. Gralnick, H., Coller, B., and Marchesi, S.: Immunological Studies of Factor VIII in Haemophilia and von Willebrand's Disease. Nature New Biology 244: 281, 1973.

4. Gralnick, H., Coller, B., and Marchesi, S.: Studies of the Human Factor VIII/von Willebrand Factor Protein. I. Comparison of the Protein Found in Normal, von Willebrand's Disease and Hemophilia A. Thromb. Res. 6: 93, 1975.

5. Gralnick H., Marchesi, S., and Coller, B.: Theoretical Approach to Molecular Biology of Factor VIII: Heterogeneity of the Molecule. Ann. NY Acad. Sci. 240: 378, 1975.

6. Coller, B., Hirschman, R., and Gralnick, H.: Studies of the Factor VIII/von Willebrand Factor Antigen on the Platelet Surface. Thromb. Res. 6: 469, 1975.

7. Gralnick, H. and Coller, B.: Studies on the Factor VIII/von Willebrand Factor Protein. II. Identification and Characterization of the von Willebrand Protein. Blood 46: 417, 1975.

8. Gralnick, H., Coller, B., and Sultan, Y.: Studies on the Human Factor VIII/von Willebrand Factor Protein. III. Qualitative Defect in von Willebrand's Disease. J. Clin. Invest. 56: 814, 1975.

9. Gralnick, H., Coller, B., and Sultan, Y.: Carbohydrate Deficiency of the Factor VIII/von Willebrand Factor Protein in von Willebrand's Disease Variants. Science 192: 56, 1976.

10. Gralnick, H. and Coller, B.: Molecular Defects in Hemophilia A and von Willebrand's Disease. Lancet, April 17, 1976.

11. Coller, B., Franza, B., Jr., and Gralnick, H.: The pH Dependence of Quantitative Ristocetin Aggregation: Theoretical and Practical Implications. A New Device for Maintenance of Platelet-Rich Plasma pH. Blood 47: 841, 1976.

12. Gralnick, H.R., Sultan, Y., and Coller, B.S.: von Willebrand's Disease Combined Qualitative and Quantitative Abnormalities. N. Engl. J. Med. 296: 1024, 1977.

13. Gralnick, H. R., Coller, B.S., Shulman, N. R., Andersen, J. C., and Hilgartner, M.: Factor VIII. Ann. Int. Med. 86: 598, 1977.

14. Coller, B.S. and Gralnick, H. R.: Studies on the Mechanism of Ristocetin-Induced Platelet Agglutination: Effects of Structural Modification of Ristocetin and Vancomycin. J. Clin. Invest. 60: 302, 1977.

15. Gralnick, H.R.: Factor VIII/von Willebrand Factor Protein: Galactose--A Cryptic Determinant of von Willebrand Factor Activity. J. Clin. Invest. 62: 496, 1978.

16. Morisato, D. and Gralnick, H.: Selective Binding of the Factor VIII/von Willebrand Factor Protein to Human Platelets. Blood 55: 9, 1980.

17. Gralnick, H., Sultant, Y., and Coller, B.: Variants of von Willebrand's Disease, In Haemostasis and Thrombosis. Edited by Serneri, G. G. N. and Prentice, C. R. M., Academic Press, Inc., New York, p. 425, 1979.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE<br>PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br><br>Z01 CL 00016-04 CP |

PERIOD COVERED
October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Qualitative Improvement of Blood Transfusion Using Young Cell Cohorts

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | |
|---|---|---|
| PI: | Laurence Corash, M.D. | Assistant Chief, Hematology Ser., CP, CC |
| Other: | H. Klein, M.D. | Assistant Chief, Blood Bank, CC |
| | A. Deisseroth, M.D. | Section Chief, Pediatric Oncology, NCI |
| | A. Nienhuis, M.D. | Chief, Clinical Hematology, NHLBI |

COOPERATING UNITS (if any)
S. Piomelli, Department of Pediatrics, Columbia University College of Physicians and Surgeons, Babies Hospital, New York, NY

LAB/BRANCH
Clinical Pathology Department

SECTION
Hematology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.8 | 0.5 | 0.3 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The purpose of this study is to demonstrate that Stractan separated young red blood cells can be transfused into autologous non-human primate donors and that these cells have an improved survival compared to whole blood. Studies have shown that young red cells from rabbits can be isolated and demonstrate a markedly improved survival compared to unfractionated whole blood. The rhesus monkey model has been developed and demonstrates that young red cells also have improved survival. The eventual goal of this project will be to explore the use of this system for human transfusion, thus reducing the transfused iron load in patients with chronic anemias. The study has been expanded to use presently available cell separates to prepare units for transfusion of young red blood cells. Units of young red cells have been isolated from normal donors and transfused into asplenic thalassemia major patients. Survival of these cells is vastly improved compared to routine frozen red cells. A small group of thalassemia major patients is now being supported with this product.

Project No. Z01 CL 00016-04 CP

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Qualitative Improvement of Blood Transfusion Using Young Cell Cohorts

Previous Serial Number: Z01 CC 00016-03

Principal Investigator: Dr. Laurence Corash

Other Investigators:
Dr. H. Klein
Dr. A. Deisseroth
Dr. A. Nienhuis

Man Years:

Total: 0.8
Professional: 0.5
Other: 0.3

## Project Description

### Objectives:

1. Development of a rhesus monkey model to examine the survival of Stractan separated age dependent red cell cohorts.

2. To determine if naturally occurring arabino-galactan antibodies exist in humans and rhesus monkeys and to determine if they develop in animals after exposure to arabino-galactan treated cells.

3. To modify existing technology, IBM and Aminco cell separators, to prepare young red cells for transfusion.

### Methods:

Age dependent red cell cohorts were obtained with arabino-galactan density gradients. Red cell life span is measured with radiochromium or radioactive cyanate. Radioimmunoassay using an iodinated myeloma protein with anti-arabino-galactan specificity. Young red cells were obtained by use of continuous flow cell separator devices.

## Major Findings:

Young red cells from rabbits have an improved survival compared to old red cells when transfused in autologous donors. Experiments in the rhesus model were similar. Young red cells were prepared and chromium 51 red cell survivals in beta thalassemia patients confirm a greatly improved red cell survival.

## Significance:

This technology may provide a means for qualitatively improved red cell transfusion, thus limiting iron overload in patients with chronic transfusion requirements. Adaptation of currently available cell separators to this basic methodology makes rapid inception of this approach readily feasible. A current transfusion program has been started by the author.

## Awards and Honors:

NIH Grant HL-19946-1. "Reduction of Iron Overload in Thalassemia"

## Publications:

1. Corash, L., Piomelli, S., Seaman, C., Comisa, C.: High Resolution Separation of Blood Cell Types by Density Gradient Centrifugation. Blood 42: 1006, 1973.

2. Corash, L., Piomelli, S., Chen, H., Seaman, C., Gross, E.: Separation of Erythrocytes According to Age on a Simplified Density Gradient. J. Lab. Clin. Med. 84: 147-151, 1974.

3. Corash, L., Seaman, C., Comisa, C., Reibman, J. R., Piomelli, S.: Separation of RBC's with Improved Survival from Normal Blood. Ped. Res. 8: 399, 1974.

4. Corash, L., Seaman, C., Reibman, J., Tytun, A, Piomelli, S.: Qualitatively Improved Blood Cell Transfusion. A New Approach to Therapy of Chronic Anemias. 16th Meeting, Int. Soc. Hem., Kyoto, Japan, 1976.

5. Piomelli, S., Seaman, C., Reibman, J., Tytun, A., Graziano, J., Tabachnick, N., Corash, L.: Separation of Younger Red Cells with Improved "In Vivo" Survival: A New Approach to Chronic Transfusion Therapy. Proc. Natl. Acad. Sci. 75: 3474-3478, 1978.

6. Corash, L., Klein, H., Deisseroth, A., Nienhuis, A.: Collection of Survival of Young Erythrocytes for Transfusion Support of Thalassemia Major Patients. Blood 54:121a, 1979.

Publications: (continued)

7. Corash, L., Klein, H., Deisseroth, A. Shafer, B., Rosen, S., Beman, J., Griffith, P., Nienhuis, A.: Selective Isolation of Young Erythrocytes for Transfusion Support of Thalassemia Major Patients, 1980 (in press).

8. Corahs, L.: Erythrocyte Fractionation by Density Gradient Centrifugation. In, Nienhuis, A. (moderator) Thalassemia Major: Molecular and Clinical Aspects. Ann. Int. Med. 91:889-892, 1979.

| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-10022-05 CP |
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PERIOD COVERED
October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Detection of Bacteremia Using an Electrical Impedance Detection System (continued study)

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: Dr. Charles H. Zierdt, Microbiologist, Microbiology Svc., CPD, CC

OTHER: Dr. James D. MacLowry, Chief, Microbiology Service, CPD, CC
Mr. Edward Hall, Engineer, B.E.I.B.
Dr. E. Arthur Robertson, Asst. Chief, Laboratory Computer Service

COOPERATING UNITS (if any)

Biomedical Engineering and Instrumentation Branch, DRS, NIH

LAB/BRANCH
Clinical Pathology Department

SECTION
Microbiology Service, Laboratory Computer Service, B.E.I.B.

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.0 | 0.25 | 0.75 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

This project has been crippled because of electronic unreliability in the impedance detection instrument and in the computer, which has had regular breakdowns and poor service. Dr. Tom Lewis has effected changes to correct this situation. The work to date has shown the promise of impedance detection of bacterial growth. Major advantages over radioactive methods are safety, economy, and freedom from disposal problems. Impedance growth curves are characteristic and reproductible for many of the test strains. This finding was unexpected and demands further investigation. Impedance response to bacterial growth as a phenomenon is complex and little understood. There are probably a number of competing electrical phenomena, and a number of ways that these affect electrodes, which become "coated" during growth, such that detection of further impedance response is severely blunted. Impedance growth curves vary greatly between bacterial species. Brucella abortus provides a very slow, steady millivolt response such that the computer does not signal the culture positive until the population density is $1x10^6$ bacteria/ml. Escherichia coli lowers impedance sufficiently at $1x10^4$/ml to signal a positive culture. Since automation is the prime consideration at this time for using impedance detection, this large difference is not critical in early growth detection, since because of continuous monitoring, even the slow response usually prompts a positive signal long before visual detection would be likely.

Project No. Z01-CL-10022-05 CP
1. Clinical Pathology Dept.
2. Microbiology Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Detection of Bacteremia Using an Electrical Impedance Detection System (continued study)

Previous Serial No.: Z01-CL-10022-04 CP

Principal Investigator: Dr. Charles H. Zierdt

Other Investigators:
Dr. James D. MacLowry
Mr. Edward Hall
Dr. E. Arthur Robertson

Man Years:
Total: 1.0
Professional: 0.25
Other: 0.75

## Project Description

### Objectives:

An attempt is being made to more rapidly detect positive clinical blood cultures in an automated fashion.

### Methods Employed:

A prototype impedance detector with a capacity for 60 blood cultures has been developed and connected to a dedicated computer in the laboratory. This represents a novel approach to detection of bacterial cultures by using a very minimum amount of human intervention. The blood has been lysed and filtered before presentation to the detector to increase bacterial yield. Thus the separate techniques of impedance detection and lysis filtration blood cultures are mated.

### Major Findings and Proposed Course:

1. Progress has been severely hampered because of electronic unreliability, both in the impedance detection-amplifier and in the PDP 11 computer, which has the task of storing and analyzing millivolt (impedance) input signals from the 60 blood culture electrode bottles. The problems with the detector have been successfully challenged, but the PDP 11 is a continuing headache, because of its unreliability. Service is not adequate. Dr. Tom Lewis is addressing the problem, and there should be an early turn around in this area.

2. Impedance lowering as bacterial growth is beginning, has definite promise as a "clean" means of early detection of positive blood cultures.

3. The impedance curves derived from strains of bacteria used to establish impedance versus growth curves have been characteristic of the species. This is an intriguing, unexpected finding, and it will receive continued investigation.

4. The mechanism of impedance changes in developing cultures is complex and little understood. There are probably a number of competing electrical phenomena, and a number of ways that these affect the electrodes, which become "coated" during growth, such that detection of further impedance response is severely blunted. The electrodes then must be scoured or flamed to red heat to restore electrode sensitivity. It is quite probable that electrode materials, construction, and coatings can be eventually selected to express particular microbial growth versus electrode impedance phenomena. It may be that within this complex array there are combinations providing species specific responses.

5. Impedance-growth curve characteristics vary greatly between species, as stated in(4). Brucella abortus, for example provides a very slow, steady quantitative response such that the computer does not signal the culture positive until the population density is 1 x $10^6$/ml. Other species, as Escherichia coli, for example, drop the impedance enough at 1 x $10^4$ colony forming units/ml to signal a positive culture. Since automation is the prime consideration at this time for using impedance detection, this large difference is not critical in early growth detection, since because of continuous measuring, even the slow response will usually prompt a positive signal long before a visual report would be likely.

## Significance to Biomedical Research and the Program of the Institute:

This methodology may enable a routine diagnostic laboratory to detect bacteremia more rapidly than with conventional means. Also it is in many ways preferable to radioactive detection methods for automation of blood cultures. It is more economical, creates no radiation hazard, and leaves no radioactive residue for disposal.

## Publications:

Zierdt, C.H., Kagan, R.L. and MacLowry, J.D.: Development of Lysis-Filtration Blood Culture Technique. J. Clin. Microbiol. 5: 46-50.

Kagan, R.L, Schuette, W.H., Zierdt, C.H. and MacLowry, J.D.: Rapid Automated Diagnosis of Bacteremia by Impedance Detection. J. Clin. Microbiol. 5: 51-57, 1977.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-100024-21 |

PERIOD COVERED
October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Analysis of 20 years of Staphylococcus aureus Bacteria Phage Typing

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Dr. Charles H. Zierdt, Microbiologist

Dr. James D. MacLowry, Chief, Microbiology Service

Dr. E. Arthur Robertson, Asst. Chief, Laboratory Computer Services

COOPERATING UNITS (if any)

None

LAB/BRANCH
Clinical Pathology Department

SECTION
Microbiology Service, Laboratory Computer Service

INSTITUTE AND LOCATION
Clinical Center, National Institutes of Health, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.0 | 0.5 | 0.5 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

1. A means has been devised of estimating numerically the relative virulence of S. aureus strains, from computer stored phage typing patterns plus the categories of infections caused. A high ratio of serious infections to simple "colonization" results in a high "Index of Infections Potential".

2. Analysis of over 20,000 phage typed S. aureus strains vis a vis infections caused has revealed that, as the phage pattern grows shorter (in the number of typing phages lysing the strain) the potential of the strain for causing infections becomes greater. Non-typable strains, long regarded as having low virulence, actually have more virulence than most strains.

PHS-6040
(Rev. 10-76)

Project No.: Z01-CL-100024-21 CP
1. Clinical Pathology Dept.
2. Microbiology Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Analysis of 20 years of Staphylococcus aureus Bacteria Phage Typing (continuing study)

Previous Serial No.: Z01-CL-100024-20 CP

Principal Investigator: Dr. Charles H. Zierdt

Other Investigators: Dr. James D. MacLowry
Dr. E. Arthur Robertson

Man Years: Total 1.0
Professional 0.5
Other 0.5

## Project Description

### Objectives:

Statistical analysis of 22,000 bacteriophage typed Staphylococcus aureus strains, from Clinical Center patients, 1957 to 1977.

### Methods Employed:

Reconstruct the epidemiology of Staphylococcus aureus infections in the Clinical Center over the past 20 years using the central DCRT computer facilities.

### Major Findings and Significance:

There is no method for estimating differences in virulence potential between Staphylococcus aureus strains. In the large, the same armamentarium of toxins is available to all S. aureus. But there is a great range in ability of S. aureus strains to initiate severe infections, as seen in hospital patients or in animal infections studies. It is necessary to be able to distinguish between strains. Phage typing does this better than any other system. From computer stored phage "finger printing" of strains, we have determined for each S. aureus strain a ratio of the number of serious infections caused to the number of "colonization" type isolations, resulting in what may be called the "Index of Infections Potential". This index ranges from about 5 for a relatively "safe" phage type of S. aureus to about 35 for typed strains causing the most infections, as septicemias, abscesses, wound infections, etc.

In addition, this study has revealed that (the latter four were in last year's report):

1. As the phage pattern grows shorter (in the number of typing phages lysing the strain) the infections potential of the S. aureus strain is greater.

2. Non-typable strains, usually regarded as having less virulence, actually have on the average, a rather high "Index of Infections Potential".

Publications:

Computer analysis of Staphylococcus aureus phage typing data from 1957 to 1975, citing epidemiological trends and natural evolution within the phage typing system.
Zierdt, C.H., Robertson, E.A., Williams, R.L. and MacLowry, J.D. Applied and Environmental Microbiology 39: 623-629 (1980).

Another paper in preparation

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 10027-02 CP |

PERIOD COVERED

October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Platelet Serotonin Metabolism

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Laurence Corash, M.D. | Assistant Chief, Hematology Ser. | CP CC |
| Other: | J. Costa, M.D. | Staff Physician | LCS,NIMH |

COOPERATING UNITS (if any)

LAB/BRANCH

Clinical Pathology Department

SECTION

Hematology Service

INSTITUTE AND LOCATION

CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.3 | 0.1 | 0.2 |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Serotonin is a vaso-active amine which is highly concentrated in the blood platelet. Release of serotonin in response to platelet activating stimuli may play a role in many pathologic states. The absence of platelet serotonin is associated with severe platelet dysfunction and a hemorrhagic diathesis. We have modified a sensitive assay to accurately measure platelet endogenous serotonin content in normal subjects and patients. Young, heavy platelets contain four times the serotonin of old, light platelets. Thus, platelet serotonin content may be a useful means to measure platelet turnover rates. Isolation of age dependent platelet cohorts permits the study of serotonin uptake, content and release in a variety of pathologic states.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10027-02 CP

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Platelet Serotonin Metabolism

Previous Project Number: Z01 CC 10027-01

Principal Investigator: Dr. Laurence Corash

Other Investigators: Dr. J. Costa .

Man Years:

| | |
|---|---|
| Total: | 0.3 |
| Professional: | 0.1 |
| Other: | 0.2 |

## Project Description

### Objectives:

1. Measurement of platelet endogenous serotonin content.

2. Quantification of serotonin storage sites and transport rates in age dependent platelet cohorts.

### Methods Employed:

Platelets were isolated by use of arabino-galactan gradients. Serotonin transport was measured by rapid uptake of radioactive serotonin and formaldehyde fixation. Serotonin content was measured by a specific double isotope dilution assay.

### Major Findings:

1. Serotonin storage sites, platelet dense bodies, are distributed in an age dependent fashion among platelets.

2. The rate of transport is equal in young and old platelets.

3. Young platelets contain four times the serotonin content of old platelets. This is due to a decreased number of storage sites.

### Significance:

Platelet serotonin is important for normal platelet function and may play a role in pathologic states that involve the platelet release reaction. The methodologies developed in this study serve to better understand these disorders.

Awards and Honors:

None

Publications:

1. Corash, L, Costa, J., Tan, H., Shafer, B., Fauci, A.S., Wolff, S.M.: 5-Hydroxytryptamine Metabolism, Alpha Granule Release and Life Span of Chediak-Higashi Syndrome Platelets. Clin. Res. 25: 337A, 1977.

2. Costa, J.L., Stark, H., Shafer, B., Corash, L., Smith, M.A., Murphy, D.L.: Maximal Packet Size for Serotonin in Storage Vesicles of Intact Human Platelets. Life Sciences 23:2193-2198, 1978.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 10028-03 CP |

PERIOD COVERED
October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Platelet Aging

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | |
|---|---|---|
| PI: | Dr. Laurence M. Corash | Assistant Chief, Hematology Service, CP, CC |
| Other: | Dr. Henry K. Tan | Palomar Memorial Hospital California |
| | Dr. Mark Perlow | Staff Fellow M SMRC |
| | Dr. Jon Costa | Staff Physician, Lab. of Neuropharmacology NIMH |
| | Dr. Dennis Murphy | Chief, Lab. of Neuropharmacology, NIMH |

COOPERATING UNITS (if any)

LAB/BRANCH
Clinical Pathology Department

SECTION
Hematology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
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| 1.0 | 0.5 | 0.5 |

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☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Blood platelets have a finite life span in the peripheral circulation and under normal steady state conditions are removed by a discrete aging process. Earlier studies had suggested that there were structural, metabolic, and functional differences between young and old platelets. Existing methods to isolate platelets for study were inadequate. An efficient method to quantatively isolate pure blood platelets has been developed in this laboratory. Experiments have shown that there is a strong relationship between platelet density and platelet structure, metabolism and function. Use of a non-human primate model has shown that these density dependent characteristics do correlate with platelet age. Thus, it is now possible to isolate age dependent platelet cohorts and to measure age dependent parameters of pure whole blood platelets. These techniques provide a means to analyze mechanisms of platelet aging to estimate platelet turnover rates, and to isolate platelets of improved quality for potential use in therapeutic transfusion. An asplenic rabbit model has been developed to look at platelet productions. Studies with this system further confirm the platelet age-density relationship.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10028-03 CP

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Platelet Aging

Previous Project Number: Z01 CL 10028-02

Principal Investigator: Dr. Laurence M. Corash

Other Investigators: Dr. Henry K. Tan
Dr. Mark Perlow
Dr. Jon Costa
Dr. Dennis Murphy

Man Years:

| | |
|---|---|
| Total: | 1.0 |
| Professional: | 0.5 |
| Other: | 0.5 |

## Project Description

Objectives:

1. Isolation of pure whole blood platelets which are structurally and functionally intact.
2. Correlation of platelet density with structure, metabolism and function.
3. Development of a sub-human primate model to prove that platelet density is an age dependent parameter.
4. Evaluation of platelet size, serotonin content and glycolytic rate as a means to estimate platelet turnover rate in patients with various platelet disorders.
5. Measurement of biochemical activity associated with different subcellular organelles: mitochondria, lysosome and dense bodies.

Methods Employed:

Platelets were isolated from whole blood and separated into density dependent cohorts by use of isosmolar arabino-galactan discontinuous gradients and ultra-centrifugation. Cell volume distribution was measured with an electronic particle counter equipped with a logarithmic amplifier and a small computer. Platelet ultrastructure was viewed with transmission electron microscopy. Platelet function was evaluated by aggregation to standard platelet stimulating agents. A sensitive double isotopic radioactive assay was adopted to measure

endogenous serotonin content. The rhesus monkey model was developed to isolate density dependent platelet cohorts which were labelled and radiochromium and reinfused into donor animals to measure cohort life span.

Monoamine oxidase activity, beta glucuronidase activity, dense body content serotonin content and transport rate as well as release were measured.

## Major Findings:

1. Pure whole blood platelets in high yield can be isolated by this technique.

2. Traditional isolation methods are biased in favor of smaller, lighter platelets.

3. Platelets can be effectively isolated from plasma proteins and then be reconstituted to a functional state with autologous plasma.

4. There is a significant correlation between platelet density and cell volume, structure and organelle content.

5. A well defined range of platelet size distribution exists and was defined for a large population of normal subjects.

6. Simultaneous platelet size determination and standard radiochromium platelet survivals were performed in patients. There is a strong correlation between decreased platelet life span and increased platelet volume.

7. The rhesus monkey model has shown that heavy platelets have a longer survival than do light platelets. Introduction of a heavy platelet cohort label into the bottom of a gradient results in progressive migration of the label up through the gradient, thus clearly demonstrating that heavy platelets become light platelets.

8. Heavy platelets contain four times the serotonin content of light platelets, thus serving as a useful age dependent marker.

9. Although platelet mitochondria number does not vary with cell age, younger platelets consistently have higher monoamine oxidase activity. Young platelets contain more dense bodies than old platelets but serotonin packet size and releasability are equivalent.

## Significance

Earlier techniques have not been able to efficiently isolated whole blood platelets. This method removes all plasma proteins from platelets which was not possible by earlier methods. For the first time age dependent platelet

cohorts from a total whole blood platelet population can be isolated. Subsequent study of these cell cohorts will permit evaluation of aging effect on platelets in disease. This method will also provide diagnostic information to discriminate diseases with increased platelet destruction from diseases with failure of platelet production. It will also facilitate studies to determine if platelet disorders are due to a qualitative protein defect or a quantitative protein defect. This study provides a new method to explore platelet aging.

Proposed Course:

The project is now being extended to apply the method to patients with platelet disorders. The animal model will be manipulated to perform in vivo experiments which cannot be performed in patients.

Honors and Awards:

None

Publications:

1. Corash, L., Gralnick, H.R.: High Yield Quantitative Isolation of Human Platelets from Whole Blood. Blood 44:919, 1974.

2. Corash, L., Tan, H., Gralnick, H.: Heterogeneity of Human Whole Blood Platelet Subpopulations. I. Relationship Between Buoyant Density, Cell Volume, and Ultrastructure. Blood 49:71-87, 1977.

3. Corash, L., Shafer, B., Weinberg, D., Steinfeld, M.B.: Platelet Sizing of Whole Blood Total Platelet Populations in Platelet Function Testing, Day, H.J., Holmsen, H., Zucker, M.D. (eds.). Dept. HEW Publication, NIH 78-1087, pp. 315-322 and pp. 773-737, 1976.

4. Andersen, J., Gralnick, H., Corash, L.: Partial Characterization of Platelet Associated Factor VIII. Circulation 54:II-115, 1976.

5. Corash, L., Costa, J., Tan, H., Shafer, B., Fauci, A.S., Wolff, S.M.: 5-Hydrozytryptamine Metabolism, Alpha Granule Release, and Life Span of Chediak-Higashi Syndrome Platelets. Clin. Res. 25:337A, 1977.

6. Norton, J.A., Shulman, N.R., Corash, L., Smith, R.L., Au, F., Rosenberg, S.A.: Severe Thrombocytopenia Following Intralesional BCG Therapy. Cancer 41:820-826, 1978.

7. Murphy, D.L., Costa, J.L., Shafer, B., Corash, L.: Monoamine Oxidase Activity in Different Density Gradient Fractions of Human Platelets. Psychopharmacology 59:193-197, 1978.

8. Goldstein, R.E., Corash, L., Capurro, N.L., Andersen, J.C., Epstein, S.E.: Decrease in Platelet Survival and Enhancement of Sympathetically Mediated Reflex Rises in Heart Rate After Abrupt Withdrawal of Propanolol. Clin. Res. 26:235A, 1978.

9. Corash, L., Costa, J.L., Shafer, B., Pettigrew, K., Murphy, D.: Platelet Organelle Content: Biochemical Activity and Relationship to Platelet Aging. Clin. Res. 26:345A, 1978.

10. Corash, L., Shafer, B., Perlow, M.: Platelet Heterogeneity: Relationship Between Buoyant Density and Cell Age. Clin. Res. 26:345A, 1978.

11. Corash, L., Shafer, B., Perlow, M.: Heterogeneity of Human Whole Blood Platelet Subpopulations. II. Use of a Sub-Human Primate Model to Analyze the Relationship Between Density and Platelet Age. Blood 52:726-734, 1978.

12. Tan, H.K., Harrison, M., Corash, L.: Demonstration of the Outer Surface of Freeze Etched Normal Human Platelets: Correlation with Buoyant Density. Br. J. Haematol. 40:289-298, 1978.

13. Costa, J.L., Stark, H., Shafer, B., Corash, L., Smith, M.A., Murphy, D.L.: Maximal Packet Size for Serotonin in Storage Vesicles of Intact Human Platelets. Life Sciences 23:2193-2198, 1978.

14. Corash, L.: Platelet Heterogeneity: Relationship Between Density and Age in The Blood Platelet in Transfusion. Jamieson, G., Greenwalt, T. (eds.), A.R. Liss, Inc., New York, 1978, pp. 79-82.

15. Corash, L.: Platelet Heterogeneity: Relevance to the Use of Platelets to Study Psychiatric Disorders. Schizophrenia Bulletin 6: 254-258, 1980.

16. Lum, L., Tubergen, D.G., Corash, L., Blaese, M.R.: Splenectomy in the Management of the thrombocytopenia of the Wiskott-Aldrich Syndrome. N. Engl. J. Med. 302:892-895, 1980.

17. Metcalfe, D.D., Corash, L.M., Kaliner, M.: Human Platelet Arysulphatases: Identification and Capacity to Destroy SRS-A. Immunology 37:723-729, 1979.

18. Corash, L., Shafer, B.: Use of Asplenic Rabbits to Demonstrate that Platelet Age and Density are Related. Clin. Res. (in press).

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NOTICE OF
INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 CL 10029-03 CP

PERIOD COVERED
October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)
Protective Effect of Vitamin E on Oxidative Related Hemolysis

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Joseph Schulman, M.D. | Chief, Medical Genetics Section | NICHD |
| | Laurence Corash, M.D. | Asst. Chief, Hematology Service, CP | CC |
| | Stephen Spielberg, M.D. | Asst. Prof., Dept. of Pharmacology<br>Johns Hopkins Medical School<br>Baltimore, Maryland | |
| | Lawrence Boxer, M.D. | Assoc. Prof., Dept. of Pediatrics<br>University of Indiana School of Medicine, Indianapolis, Indiana | |

COOPERATING UNITS (if any)
Johns Hopkins University Medical School
University of Indiana School of Medicine

LAB/BRANCH
Clinical Pathology Department

SECTION
Hematology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

TOTAL MANYEARS: 0.4
PROFESSIONAL: 0.4
OTHER:

CHECK APPROPRIATE BOX(ES)
☒ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☒ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Patients with chronic hemolysis due to defects in production of reduced glutathione or reduced nucleotides are being treated with large doses of vitamin E. It is postulated that vitamin E can act as a free radical scavenger and provide a partial protective effect against oxidative related hemolysis in this group of patients. Red cell survival pre- and post-therapy, as well as routine hematologic parameters and clinical course, are being monitored to evaluate the efficacy of this therapeutic approach. A large clinical trial of high dose vitamin E therapy has been completed in Greek Mediterranean type glucose-6-phosphate dehydrogenase deficient subjects. A second study in 46 patients from Beersheba, Israel with mediterroneon type G6PD deficiency was initiated. An additional 8 patients with sever chronic hemolysis due to G6PD deficiency have been entered into a study at the NIH.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10029-03 CP

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Protective Effect of Vitamin E on Oxidative Related Hemolysis
Previous Project No.: Z01 CL 10029-02
Principal Investigator: Dr. Laurence M. Corash

Other Investigators: Dr. Joseph Schulman
Dr. Stephen Spielberg
Dr. Lawrence Boxer

Man Years:

| | |
|---|---|
| Total: | 0.4 |
| Professional: | 0.4 |
| Other: | |

## Project Description

### Objectives:

To determine if oral high dose vitamin E therapy can increase red cell survival in patients with defects in reduced nucleotide or reduced glutathione production disorders.

### Methods Employed:

Routine hematologic studies are used to assess clinical status. Red cell survival studies are performed using autologous radiochromated red cells. Clinical status and red cell survival are measured before and after three months of therapy.

### Major Findings:

One patient with severe chronic hemolysis due to G6PD deficiency showed improvement with therapy. A second patients with glutathione synthetase deficiency was also improved with vitamin E therapy. Thirty-eight patients with G6PD deficiency of the Mediterranean type were entered into a cooperative study with this laboratory and Dr. C. Bartsocas, Athens, Greece. This study was completed and demonstrated a significant reduction in degree of chronic hemolysis with therapy.

### Significance:

Severe hemolysis due to oxidative stress occurs in patients with red cell deficiencies of reduced nucleotides or glutathione. These hemolytic crises may result. in death or contribute to associated disorders. Eighty million

people are affected by G6PD deficiency. High dose vitamin E therapy may offer a protective effect to these patients against oxidative stresses with subsequent hemolysis. The ultimate goal of this therapy will be to reduce both mortality and morbidity.

Proposed Course:

Studies in severely affected patients with chronic hemolysis will be extended. The Greek study in patients with episodic hemolysis will be completed and if warranted a large scale multicenter trial will be initiated.

Publications:

1. Spielberg, S.P., Garrick, M.D., Corash, L.M., Butler, J.D., Tietze, F., Rodgers, L., Schulman, J.: Biochemical Heterogeneity in Human Glutathione Synthetase Deficiency. J. Clin. Invest. 62:1417-1420, 1978.

2. Spielberg, S.P., Boxer, L.A., Corash, L.M., Schulman, J.D.: Improved Erythrocyte Survival with High Dose Vitamin E in Chronic Hemolyzing G6PD and Glutathione Synthetase Deficiencies. Ann. Int. Med. 90:53-54, 1979.
3. Corash, L., Spielberg, S., Bartsocas, C., Boxer, L., Sheetz, M., Steinherz, R., Schulman, J.D.: Reduced Chronic Hemolysis in Mediterranean Glucose-6-Phosphate Dehydrogenase Deficiency After Vitamin E Therapy. Clin. Res. 27:291A, 1979.

4. Schulman, J.D., Corash, L., Bartsocas, C., Spielberg, S., Boxer, L., Sheetz, M., Steinherz, R. and Papadatos, C.: Reduced Chronic Hemolysis in Mediterranean Glucose-6-Phosphate Dehydrogenase Deficiency After Vitamin E Therapy. Proc. of the Second International Clinical Genetics Seminar: Management of Genetic Disorders (Athens, Greece), A.R. Liss, Inc., New York, June 4-7, 1979.

5. Corash, L: Vitamin E in the treatment of hemolysis due to G-6PD deficiency. In Schulman, J.D. (moderator): Genetic disorders of glutathione and sulfur amino acid metabolism - New biochemical insights and therapeutic approaches. Ann. Int. Med. (in press).

6. Corash, L, Spielberg, S., Bartsocas, C., Boxer, L., Steinberg, R., Sheetz, M., Egan, M., Schlessleman, J. and Schulman, J.D.: Reduced chronic hemolysis during high dose vitamin E administration in Mediterranean type glucose 6 phosphate dehydrogenase deficiency. N. Engl. J. Med. (in press).

MITHSONIAN SCIENCE INFORMATION EXCHANGE
PROJECT NUMBER (Do NOT use this space)

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NOTICE OF
INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CL-10030-03

PERIOD COVERED
[illegible]er 1, 1979 through September 30, 1980

[illegible]F PROJECT (80 characters or less)

[illegible]al Deoxynucleotidyl Transferase Assays and Disease Correlations

[illegible], LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER [illegible]FESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| I: | Dr. Jerome A. Donlon | Staff, Hematology Service, CP | CC |
| Other: | Dr. Fred Bollum | Chairman, Biochemistry Dept., | USUHS |
| | Dr. David Poplack | Staff, Pediatric Oncology, | NCI |

COOPERATING UNITS (if any)
Pediatric Oncology Branch, NCI
Department of Biochemistry, USUHS

LAB/BRANCH
Clinical Pathology Department

SECTION
[illegible]matology Service

[illegible]TITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

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| TOTAL MANYEARS: 0.15 | PROFESSIONAL: 0.10 | OTHER: 0.05 |

CHECK APPROPRIATE BOX(ES)

(a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

(a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Terminal deoxynucleotidyl transferase (TdT) has been shown to be an effective biochemical marker for lymphoblastic cells in normal thymus acute lymphoblastic leukemia (ALL) and lymphoblastic leukemias. The enzyme TdT can be assayed for as an enzyme activity or by an indirect fluorescent antibody procedure. This current project attempted to compare the sensitivity of the two methods of determining the TdT enzyme. In addition, peripheral blood smears, bone marrow aspirate smears and cytocentrifuge slide preparations from a wide variety of diseases as well as normal donors were surveyed for TdT to determine its level in various diseases. Attempts at developing a PAP immunohistochmical assay for localizing TdT in tissue sections was unsuccessful. A commercially available immunofluorescent assay kit for TdT was evaluated and found acceptable.

Project No. Z01 CL-10030-03

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Terminal Deoxynucleotidyl Transferase Assays and Disease Correlations

Previous Project No.: Z01 CL-10030-02

Principal Investigator: Dr. Jerome A. Donlon

Other Investigators: Dr. Fred Bollum
Dr. David Poplack

Man Years:
Total: 0.15
Professional: 0.10
Other: 0.05

## Project Description

### Objectives:

1. To establish the validity and usefulness of an indirect fluorescent antibody assay for TdT as compared to the enzyme activity assay.

2. To obtain a broad experience with TdT assays to assess its clinical relevance in diagnosis and prognosis of various diseases.

### Methods Employed:

1. Indirect fluorescent antibody procedure for peripheral blood, bone marrow aspirate and cytocentrifuge smears.

2. Enzyme activity assay for TdT by radioisotope tracer incorporation.

### Major Findings:

1. Indirect fluorescent antibody assays and enzyme activity assays show comparable sensitivities for TdT.

2. A commercially available immunofluorescent assay kit for TdT gave comparable results to the current assay system used in Dr. Bollum's laboratory.

3. The TdT activity is decreased and often undetectable in T cell ALL as compared to the high TdT activity found in common (null cell) ALL.

4. Occasional slight elevations of TdT activity have been noted in bone marrow aspirations from patients with rhabdomyosarcoma.

Significance to Biomedical Research and to the Program of the Department:

1. The indirect fluoresecent antibody assay is sensitive and easily applied to routinely obtained slide specimens.

2. The T cell ALL has a poorer clinical prognosis, therefore in addition to the surface marker, a low or absent TdT activity would confirm this poor prognosis. Possibly chemotherapy protocols can be adjusted if an ALL is found to be a T cell or low TdT type.

3. High TdT activity is possibly associated with more primitive lymphoblasts, whereas the low TdT activity may occur as the cell become more differentiated, expressing the T surface marker.

Honors an Awards:

None

Publications:

None

| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 10031-03 CP |
|---|---|---|

PERIOD COVERED

October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

A Clinico-Pathologic Study of the Hypereosinophilic Syndrome

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | |
|---|---|---|
| PI: | Dr. Harvey R. Gralnick | Chief, Hematology Service, CPD, CC |
| Other: | Dr. Anthony Fauci | Staff, Lab. Clin. Invest. NIAID |
| | Dr. John Harley | Clinical Associate, NIAID |

COOPERATING UNITS (if any)

LAB/BRANCH

Clinical Pathology Department

SECTION

Hematology Service

INSTITUTE AND LOCATION

CC, NIH, Bethesda, MD 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 3.5 | 3.5 | |

CHECK APPROPRIATE BOX(ES)

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☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The bone marrows of patients seen at the Clinical Center with Hypereosinophilic Syndrome were reviewed. This was done in an attempt to correlate the bone marrows and other hematologic parameters with the patient's clinical course and response to therapy.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10031-03 CP

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: A Clinico-Pathologic Study of the Hypereosinophilic Syndrome

Previous Project Number: Z01 CL 10031-02 CP

Principal Investigator: Dr. Harvey R. Gralnick

Man Years:

| | |
|---|---|
| Total: | 3.5 |
| Professional: | 3.5 |
| Other: | 0.0 |

## Project Description

### Objectives:

To determine whether hematologic manifestations of the hypereosinophilic syndrome can be used to correlate with 1) the clinical course of the patient and, 2) response to therapy.

### Methods Employed:

The bone marrows of 32 patients were reviewed microscopically. All other hematologic data were also systematically reviewed.

### Major Findings:

Patient subgroups, defined by response to therapeutic intervention, can be predicted by initial hematologic evaluation.

### Significance:

Since a patient's response to therapy, and thus prognosis, can be defined at initial evaluation, more rational therapeutic intervention can be planned. Alternatives to present management can also be considered.

### Proposed Course:

Clinical correlates with response to therapy are being determined and will be correlated with the hematologic classification.

### Honors and Awards:

None

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-10032-03 CP |

PERIOD COVERED

October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

The Localization and Functional Significance of Platelet Membrane-Bound Factor VIII

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | | |
|---|---|---|---|---|
| PI: | Dr. Morris A. Flaum | Clinical Associate, Hematology Ser., | CP | CC |
| Other: | Dr. Margaret E. Rick | Staff, Hematology Service, | CP | CC |
| | Dr. Harvey R. Gralnick | Chief, Hematology Service, | CP | CC |

COOPERATING UNITS (if any)

LAB/BRANCH

Clinical Pathology Department

SECTION

Hematology Service

INSTITUTE AND LOCATION

CC, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS: 0.55 | PROFESSIONAL: 0.4 | OTHER: 0.15 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The role of platelet membrane-bound factor VIII is being pursued by using factor VIII antibodies as a probe. Antibodies to the low molecular weight and high molecular weight components of factor VIII are purified and used to localize factor VIII antigens on the platelet membrane by immunofluorescence. The functional significance of these fragments is then determined by platelet aggregometry with ristocetin.

PHS-6040
(Rev. 10-76)

Project No. Z01-CL-10032-03 CP

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: The Localization and Functional Significance of Platelet Membrane-Bound Factor VIII

Previous Serial Number: Z01-CL-10032- 02 CP

Principal Investigator: Dr. Morris A. Flaum

Other Investigators:
Dr. Margaret E. Rick
Dr. Harvey R. Gralnick

Man Years:

| | |
|---|---|
| Total | 0.55 |
| Professional: | 0.4 |
| Other: | 0.15 |

## Project Description

### Objectives:

To determine the role of platelet membrane-bound factor VIII.

### Methods Employed:

The localization and determination of the functional significance of factor VIII is being pursued by using factor VIII antibodies as probes. The antibodies, obtained from humans, goats and rabbits, is incubated with fresh or formalinized platelets and immunofluorescence performed. The antibodies have been demonstrated to react with either the low or high molecular weight factor VIII components in other systems. Ristocetin cofactor activity is determined by tilt-tube and aggregometry with platelets pre-incubated with these antibodies.

### Major Findings:

Factor VIII related antigen (VIII R:Ag) was identified on platelet membranes, but factor VIII coagulant antigen (VIII C:Ag) could not be identified by these techniques. VIII R:Ag appears to be present on the surface of platelets and identification does not require release from platelets. The functional role of VIII R:Ag remains elusive, since antibodies to platelet VIII R:Ag did not inhibit ristocetin-induced platelet aggregation.

Significance:

The role of platelet membrane VIII R:Ag remains unclear. It appears that the plasma level of this factor VIII component is of greater importance in the interaction of platelets and subendothelial elements in primary hemostasis. This provides some explanation for the bleeding in patients with von Willebrand's disease who have normal levels of VIII R:Ag in their platelets.

Proposed Course:

Further studies to clarify the functional significance of platelet membrane bound factor VIII are now actively being pursued.

Honors and Awards:

None

Publications:

1. Flaum, M.A., Rick, M.E., Gralnick, H.R.: The functional significance of factor VIII components in normal platelets (abstract) Blood (Suppl. 1) 54:239a, 1979.

2. Flaum, M.A., Rick, M.E., Gralnick, H.R.: The functional significance of factor VIII components in normal platelets. (submitted for publication).

| | | |
|---|---|---|
| ITHSONIAN SCIENCE INFORMATION EXCHANGE<br>ROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 10034-03 CP |

ERIOD COVERED

October 1, 1979 through September 30, 1980

TLE OF PROJECT (80 characters or less)

Thrombin Activation of Factor VIII

AMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER ROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: Dr. Margaret E. Rick Staff Physician CP CC

OOPERATING UNITS (if any)

LAB/BRANCH

Clinical Pathology Department, Clinical Center

SECTION

Hematology Service

INSTITUTE AND LOCATION

CP, CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.5 | 0.10 | 0.10 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

This investigation seeks to characterize the interaction of the factor VIII complex with thrombin, in particular the biochemical mechanism by which thrombin activates factor VIII procoagulant activity and subsequently inactivates the activity. An understanding of the regulatory role of this interaction in normal hemostasis will lead to a better understanding of the basic hemostatic process and of the functional defects in the factor VIII deficiency diseases (Hemophilia A and von Willebrand's disease) as well as in pathologic thrombotic states.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10034-03 CP

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Thrombin Activation of Factor VIII

Previous Serial No.: Z01 CL 10034-02 CP

Principal Investigator: Dr. Margaret E. Rick

Man Years:

| | |
|---|---|
| Total: | 1.5 |
| Professional: | 0.10 |
| Other: | 0.10 |

## Project Description

### Objectives:

To characterize the biochemical interaction of thrombin and factor VIII and relate this to the functional change in factor VIII procoagulant activity.

### Methods Employed:

Purified human factor VIII is obtained by differential PEG precipitation of factor VIII concentrates followed by agarose gel filtration. A low molecular weight factor VIII procoagulant is obtained by gel filtration of purified factor VIII buffers containing 0.24 M $CaCl_2$. Thrombin interaction with the factor VIII preparations is assessed with factor VIII procoagulant assays. Inhibitors of thrombin (hirudin, DFP, heparin) are employed in studying various aspects of the interaction.

### Major Findings:

The reaction patterns of thrombin with purified factor VIII and the calcium dissociated low molecular weight factor VIII are similar, demonstrating an initial increase in factor VIII activity followed by a decay of procoagulant activity. The extent of activation which is observed in the initial phase decreases with lower temperatures and with lower thrombin concentrations. A pseudo-first order relationship is demonstrated for the activation phase. The labile factor VIII procoagulant activity produced by thrombin action cannot be stabilized by the addition of inhibitors of thrombin and thus appears to be intrinsically labile. Further studies have indicated that there is product inhibition of the reaction of thrombin with factor VIII.

## Significance to Biomedical Research and the Program of the Department:

The goal of this research is to gain a better understanding of the function of factor VIII in normal hemostasis, in factor VIII deficiency diseases, and in pathologic thrombotic states. The important regulatory role of thrombin in factor VIII function will lead to a better understanding of regulation in normal hemostasis and may allow therapeutic manipulation by pharmacologic agents in thrombotic diseases.

## Honors and Awards:

None

## Publications:

1. Rick, M.E., and Hoyer, L.W.: Immunologic studies of antihemophilic factor (AHF, factor VIII). V. Immunologic properties of AHF subunits produced by salt dissociation. Blood 42:737-747, 1973.
2. Rick, M.E., and Hoyer, L.W.: Thrombin activation of low molecular weight antihemophilic factor (factor VIII). Nature 252:404, 1974.
3. Rick, M.E., and Hoyer, L.W.: Interaction of thrombin and factor VIII: I. The role of protease inhibitors. Br. J. Haematol. 36:585-597, 1977.
4. Mundy, G.R., Rick, M.E., Turcotte, B.A., Kowalski, M.A.: Hypercalcemia in lymphosarcoma cell leukemia. Am. J. Med. 65:600-605, 1978.
5. Rick, M.E., and Hoyer, L.W.: Thrombin activation of factor VIII. II. A comparison of purified factor VIII and the low molecular weight factor VIII procoagulant. Br. J. Haematol. 38:107-119, 1978.
6. Rick, M.E.: Biochemistry of blood coagulation, in The Science and Practice of Clinical Medicine, Chapter 75, V.J. Marder (ed.), Grune and Stratton, Inc., New York, 1979.
7. Rick, M.E.: Hemophilia and von Willebrand's disease, in The Science and Practice of Clinical Medicine, Chapter 80, V.J. Marder (ed.), Grune and Stratton, Inc., New York, 1978.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE<br>PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br><br>Z01 CL 10035-03-CP |

PERIOD COVERED
October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Factor VIII Interaction with Other Coagulation Factors

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: Dr. Margaret E. Rick Staff, Hematology Service, CPD, CC

COOPERATING UNITS (if any)

LAB/BRANCH
Clinical Pathology Department

SECTION
Hematology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.25 | 0.50 | 0.75 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

This project seeks to investigate the interaction of factor VIII with other coagulation factors, particularly with factor $IX_a$, calcium, and phospholipid in the quaternary complex formed by these factors. The importance of proteolytic activation of factor VIII prior to its participation in the complex will be assessed, and the nonfunctional factor VIII molecule present in patients with hemophilia A will be studied to determine whether it can participate in the quaternary complex.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10035-03 CP

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Factor VIII Interaction with other Coagulation Factors.

Previous Project No.: Z01 CL 10035-02

Principal Investigator: Dr. Margaret E. Rick

Man Years:

| | |
|---|---|
| Total: | 1.25 |
| Professional: | 0.50 |
| Other: | 0.75 |

## Project Description

### Objectives:

To characterize the interaction of factor $IX_a$ with factor VIII and the low molecular weight factor VIII procoagulant, assessing any "activation" of factor VIII procoagulant activity by factor $IX_a$ and developing an affinity reagent to study components of the quaternary complex (factor VIII, factor $IX_a$, calcium, phospholipid).

### Methods Employed:

Purified human factor VIII is obtained by differential PEG precipitation of factor VIII concentrates followed by agarose gel filtration. A low molecular weight factor VIII procoagulant is obtained by gel filtration of purified factor VIII with buffers containing 0.24 M $CaCl_2$. Factor IX is purified by barium citrate adsorption and elution, ion exchange chromatography, and affinity chromatography. Activation of factor VIII is assessed by procoagulant assay and the quaternary complex will be assessed using solid phase factor IX as an affinity reagent. Radioimmunoassays for factor VIII coagulant antigen and factor VIII related antigen are utilized to assess complex formation.

### Major Findings:

Studies indicate that bovine factor $IX_a$ activates purified human factor VIII at near stoichiometric concentrations of the reactants. Factor VIII activity is enhanced five-fold and is followed by a decay of the activity which follows pseudo-first order reaction kinetics. The reaction is optimal at $37^{\circ}C$ and is increased in the presence of phospholipid.

Significance to Biomedical Research and the Program of the Department:

The goal of this research is to gain a better understanding of the function of factor VIII in normal hemostasis and in the factor VIII deficiency diseases (Hemophilia A and von Willebrand's disease). The role of the respective components within the quaternary complex will provide insights into the normal function of factor VIII and the possible mechanism of dysfunction in the factor VIII deficiency diseases.

Honors and Awards:

None

Publications:

Rick, M.E., Pike, S.E.: Activation of factor VIII by factor $IX_a$. Clin. Res. 28:321A, 1980.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>**NOTICE OF**<br>**INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 10036-03 CP |

PERIOD COVERED
October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)
Evaluation of the Limulus Lysate Test

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | |
|---|---|
| Principal Investigator: | Ronald J. Elin, Chief, Clinical Pathol. Dept., CC |
| Others: | Harold Nishi, Senior Staff, Chemistry Serv., CPD,CC |

COOPERATING UNITS (if any)
None

LAB/BRANCH
Clinical Pathology Department

SECTION
Clinical Chemistry Service

INSTITUTE AND LOCATION
National Institutes of Health, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 2 | 1 | 1 |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The limulus lysate test is currently the most sensitive assay for the detection of bacterial endotoxin. The sensitivity and specificity of the limulus test for the detection of bacterial endotoxin in blood, cerebral spinal fluid, joint fluid and urine in man have been and are being evaluated to determine the clinical utility of this assay. Compounds other than bacterial endotoxin that can cause a positive limulus reaction are being characterized. A nephelometric method for performing the limulus assay to enhance sensitivity and specificity is being developed.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10036-03
1. Clinical Pathology Department
2. Clinical Chemistry Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 to September 30, 1980

Project Title: Evaluation of the Limulus Lysate Test

Previous Serial No.: Z01 CL 10036-02

Principal Investigator: Dr. Ronald J. Elin

Other Investigator: Mr. Harold Nishi

Cooperating Units: None

| | | |
|---|---|---|
| Man Years: | Total | 1.0 |
| | Professional | 0.25 |
| | Other | 0.75 |

## Project Description

Objectives:

To determine the specificity, clinical utility and optimum method for performance of the limulus assay.

Methods Employed:

The limulus assay was performed by mixing lysate with the test material and determining if gelation occurred. The assay was also performed using a nephelometer.

Major Findings:

The limulus assay is not specific for the detection of bacterial endotoxin in joint fluid or plasma from humans. The test does have clinical utility for the detection of bacterial endotoxin in cerebral spinal fluid. It appears that an elevated neutrophil count may affect a positive limulus test. In addition, Poly (I) · Poly (C) was shown to unequivocally effect a positive limulus test. Thus, this is one of several compounds other than bacterial endotoxins which can cause a positive limulus test.

Significance:

The use of the limulus test for the detection of bacterial endotoxin in plasma in joint fluid is not recommended. The test does have clinical utility for the detection of bacterial endotoxin in cerebral spinal fluid.

Honors and Awards: None

Publications:

Hochstein, H. D., Elin, R. J., Cooper, J. F., Seligman, E. B., Jr., and Wolff, S. M.: Further developments of limulus amebocyte lysate test. Bull. Parenteral Drug Assoc: 27: 139-148, May-June 1973.

Elin, R. J., Robinson, R. A., Levine, A. S., and Wolff, S. M.: Lack of clinical usefulness of the limulus test for the diagnosis of endotoxemia. N. Engl. J. Med: 293: 521-524, September 1975.

Elin, R. J., Sandberg, A. L., and Rosenstreich, D. L.: Comparison of the pyrogenicity, limulus activity, mitogenicity and complement reactivity of several bacterail endotoxins and related compounds. J. Immunology. 117: 1238-1242, October 1976.

Elin, R. J., Knowles, R., Barth, W. F., and Wolff, S. M.: Lack of specificity of the limulus lysate test in the diagnosis of pyrogenic arthritis. J. Infect. Dis. 137: 507-513, 1978.

Publications: (Continued)

Elin, R. J., Clinical utility of the limulus test with blood, CSF and synovial fluid. In Cohan, E. (ed.): Biomedical Applications of Limulus Polyphemus. Alan R. Liss, Inc., New York. 1979.

Elin, R. J. and Utter, A.: Positive limulus amebocyte lysate reactions with Poly (I) • Poly (C). J. Clin. Microbiol. In Press.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-10044 02 CP |

PERIOD COVERED

October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Lysis-Filtration Blood Culture Technique (continuing study)

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: Dr. Charles H. Zierdt, Microbiologist, Microbiology Service, CPD, CC

Other: Dr. James D. MacLowry, Chief, Microbiology Service, CPD, CC

COOPERATING UNITS (if any)

None

LAB/BRANCH

Clinical Pathology Department

SECTION

Microbiology Service

INSTITUTE AND LOCATION

CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.0 | 0.25 | 0.75 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A year of development and testing has resulted in a simplified human blood lysing solution, comprising distilled water, 1% Rhozyme P-11, and 0.5% Tween 20. This new solution lyses erythrocytes, kills phagocytes and releases contained bacteria, and reduces the viscosity of the blood. The latter effect is necessary to permit filtration without filter clogging. Thorough testing has shown the new lysing solution to be non-injurious over two hours time to all bacterial pathogens tested, including those most sensitive to the former Triton X-100 based solution, i.e., *Neisseria meningitidis*. The study now is directed to testing, by lysis-filtration, large series of blood samples from patients, for bacterial recovery, in direct comparison with conventional blood culture techniques. During the same period, animal experiments will be done (in rabbits), creating low-grade septicemia and then testing the relative bacterial recovery sensitivity of lysis-filtration culture versus conventional culture.

PHS-
(Rev.

Project No. Z01-CL-10044 02 CP
1. Clinical Pathology Dept.
2. Microbiology Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Lysis-Filtration Blood Culture Technique (continuing study)

Previous Serial No.: Z01-CL-10044 01

Principal Investigator: Dr. Charles H. Zierdt

Other Investigators: Dr. James D. MacLowry

Man Years:
Total: 1.0
Professional: 0.25
Other: 0.75

## Project Description

### Objectives

Continue to develop and improve the existing successful technique for this radically different blood culturing technique. In addition to collecting data from clinical studies, animal studies are in progress to provide controlled experiments comparing the relative abilities of the conventional and the lysis filtration blood culture techniques to recover pathogenic microorganisms from blood.

### Methods Employed:

Lysis of blood with a simpler solution containing 1% Rhozyme (protease mixture), 0.5% Tween 20, and distilled water.

### Major findings and significance:

The earlier lysing solution, while successful, nevertheless was overly damaging to a few rare blood pathogens, particularly *Neisseria meningitidis*. This was because of its content of 0.04% Triton X-100. The new simplified formula (see Methods) replaces Triton X-100 with nonionic Tween 20 (polyoxyethylenesorbitan monolaurate). The new solution lyses erythrocytes and also destroys white cells, while releasing contained bacteria. It has no killing effect on *Neisseria meningitidis* or any bacterial pathogen tested.

Proposed course:

To test the new formula on recovery of pathogens from patients blood samples. Also, blood samples from rabbits with experimental septicemias will be cultured by lysis-filtration and conventional blood culture in a direct comparison of the two systems. Preliminary tests in rabbits indicate that the lysis filtration technique is far more sensitive than the conventional blood culture in detecting *Staphylococcus epidermidis* bacteremia.

Publications:

Zierdt, C.H., Kagan, R.L. and MacLowry, M.D.: Development of a Lysis-Filtration Blood Culture Technique. *J. Clin. Microbiol.* 5: 46-50, 1977.

New data in preparation for publication.

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|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE<br>PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-10045-02 CP |

PERIOD COVERED
October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Evaluation of Throat Gram Smears

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: Dr. Vee L. Gill, Microbiologist, Microbiology Service, CPD, CC

COOPERATING UNITS (if any)

None

LAB/BRANCH
Clinical Pathology Department

SECTION
Microbiology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.5 | 0.75 | 0.25 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Throat swabs submitted for routine culture had Gram stains performed on them also. These were read without prior knowledge of cultural results and scored for the presence or absence of group A-beta hemolytic streptococcal infection, using the criteria of Crawford, et.al. (Ann. Int. Med., 90: 293-297, 1979.)

PHS-6
(Rev.

Project No. Z01-CL-10045-02 CP
1. Clinical Center, Clinical Pathology Department
2. Microbiology Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 throughSeptember 30, 1980

Project Title: Evaluation of Throat Gram Smears

Previous Serial No.: Z01 CL 10045 01 CP

Principal Investigator: Dr. Vee L. Gill

Man Years:
Total: 0.5
Professional: 0.75
Other: 0.25

## Project Description

### Objectives:

To determine the usefulness of the throat gram stain as a predictor of streptococcal sore throat.

### Methods Employed:

Criteria of Crawford et.al. were used. All throat swabs submitted for routine culture also had smears done. These smears were collected and read independently by one microbiologist.

### Major Findings:

Two hundred thirty-three throat Gram mears were reviewed by one microbiologist using the criteria of Crawford et al to predict the presence or absence of Group A streptococci. Calculation of sensitivity, specificity, and predictive value according to their definitions yielded values of 63%, 95% and 48%. Analogous values found by Crawford et al were 73%, 96% and 71%. Because of our findings of relatively low sensitivity and particularly low predictive value of the throat Gram smear procedure, no further investigations are anticipated.

### Significance to Biomedical Research and the Program of the Institute:

Since the publication of Crawford et al, the laboratory has had questions regarding the potential use of this rapid technique for predicting streptococcal pharyngitis.

We attempted to determine the usefulness of this procedure for routine laboratory work. Our results did not support the incorporation of a routine throat Gram smear for laboratory use.

Publications:

None

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE<br>**NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01-CL-10046-02 CP |

PERIOD COVERED

October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Significance of Anaerobic Bacteria from Patient Specimens

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: Dr. Vee L. Gill, Microbiologist, Microbiology Service, CPD, CC

OTHER: Dr. Kathleen Sazama, M.D., Clinical Pathology Resident, Microbiology Service, CPD, CC

COOPERATING UNITS (if any)

None

LAB/BRANCH

Clinical Pathology Department

SECTION

Microbiology Service

INSTITUTE AND LOCATION

CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1 | 0.75 | 0.25 |

CHECK APPROPRIATE BOX(ES)

__ (a) HUMAN SUBJECTS __ (b) HUMAN TISSUES x (c) NEITHER

__ (a1) MINORS __ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Patients from which anaerobic bacteria are isolated will have their charts reviewed and physicians consulted to determine the clinical significance of the isolates. Follow-up will include the nature of the treatment, if any, and clinical response. These results should guide our laboratory as well as others to determine how much anaerobic work is necessary for optimum patient care.

Project No. Z01-CL-10046-02 CP

1. Clinical Center, Clinical Pathology Department
2. Microbiology Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Significance of Anaerobic Bacteria from Patient Specimens

Previous Serial Number: Zol-CL-10046-01 CP

Principal Investigator: Dr. Vee L. Gill
Other Investigator: Dr. Kathleen Sazama

Man Years:
Total: 1
Professional: 0.75
Other: 0.25

## Project Description

### Objectives:

To assess the significance of anaerobes isolated from patient specimens. Information is needed regarding the specific organisms and their role in infection, as well as the clinical usefulness of providing anaerobic culturing.

### Methods Employed:

All wounds, abscesses, lesions and drainage materials are cultured for anaerobes. Full anaerobic work-up is done on most anaerobes isolated. Patients' charts will be reviewed and their physician spoken with, when relevant, to determine the role of these anaerobes.

## Major Findings:

Information on 23 patients from whom anaerobic organisms were isolated was collected and reviewed. Specimens from which the anaerobes were isolated were ulcers, wounds, abscesses, incision sites, and drainage fluids. In 22 of 23, the physician's impression was that of infection or superinfection of these sites. In only 4 instances was the possibility of anaerobic infection mentioned; 3 of these were placed on clindamycin. An additional 2 patients were placed on clindamycin presumably for the possibility of anaerobes, although no specific mention was made of this. All sites either had been or were open and draining. Nineteen of the 23 patients were placed on antibiotics; a semisynthetic penicillin, gentamicin, clindamycin and/or a cephalosporin were the most commonly used. Twenty-two of the 23 grew aerobic organisms, 19 of which included significant potential pathogens, including *Pseudomonas aeruginosa*, *Staphylococcus aureus*, Group D streptococci, *Escherichia coli*, and *Klebsiella pneumoniae*. Of the anaerobes, anaerobic gram positive cocci, *Peptococcus* or *Peptostreptococcus*, were the most common, occurring in 17/23 patients, *Bacteroides* (8/23) was next in frequency.

No change in antibiotic coverage occurred as a result of receiving a report of anaerobes present in the culture. Thus although no clindamycin or chloramphenicol was started, neither was clindamycin dropped in any case that it had already been started. The majority of patients were on antibiotics (other than clindamycin or chloramphenicol) which were probably at least partially effective against their specific anaerobes.

Five patients had no significant aerobic bacteria; all 5 had *Peptococcus*/*Peptostreptococcus* as the only anaerobic bacteria and all 5 resolved without significant sequelae. Four of these patients were on antibiotics which were probably at least partially effective against these organisms. The other 18 patients included 14 on antibiotics and 4 on no antibiotics; 11 of the former and 3 of the latter eventually resolved their infection. Four patients went on to have recurrent infection of the same site. The majority of the patients on antibiotics were not on clindamycin or chloramphenicol but were on antibiotics that had the potential of being partially effective against the specific anaerobes isolated.

## Significance:

To assess the role of anaerobes in significant infections of Clinical Center patients. This study will help to define which anaerobes are most commonly found and how often their precence appears to be of clinical concern.

Proposed Course:

Information on the first 23 patients has shown that modification of the original criteria for inclusion into this study would be useful at this juncture, particularly to include only those patients with "new" infections, and to try and collect more data on patients with no significant aerobes.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-10048-02 CP |

PERIOD COVERED
October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Evaluation of a Simplified Disc Antibiotic Susceptibility Test

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: Dr. Frank G. Witebsky, Asst. Chief, Microbiology Service, CPD, CC

OTHER: Dr. James D. MacLowry, Chief, Microbiology Service, CPD, CC

COOPERATING UNITS (if any)

None

LAB/BRANCH
Clinical Pathology Department

SECTION
Microbiology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.1 | 0.1 | 0 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Antibiotic susceptibility testing is most commonly performed using a disc diffusion method. The procedure requires extremely, careful standardization and quality control, and diameters of zones of inhibition around the discs are often difficult to read because of the manner of plate inoculation. A simplified procedure of inoculum preparation, which also provides zone edges which are much easier to read, was investigated and compared with the standard procedure.

PHS-6040
(Rev. 10-76)

Project No. Z01-CL-10048-02 CP

1. Clinical Center, Clinical Pathology Department
2. Microbiology Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Evaluation of a Simplified Disc Antibiotic Susceptibility Test

Previous Serial Number: Z01 CL 10048 01 CP

Principal Investigator: Dr. Frank G. Witebsky
Other Investigator: Dr. James D. MacLowry

Man Years:
- Total: 0.1
- Professional: 0.1
- Other: 0

## Project Description

### Objectives:

The objective of this study was the development and evaluation of a simplified disc diffusion antibiotic susceptibility testing procedure, in which the inoculum would be easier to prepare and the edges of the zones of inhibition easier to read.

### Methods Employed:

Antibiotic susceptibility testing plates were flooded with a 1:1000 dilution of a turbid broth suspension of the organisms to be tested; residual broth was aspirated from the plates and the usual susceptibility testing discs are applied. Zones of growth inhibition were read after 18-24 hours of incubation at 37°C. Parallel testing using the same organisms was performed using the standard Bauer-Kirby procedure.

### Major Findings:

This procedure has already been found useful as a part of our susceptibility testing procedures, but the disc testing aspect was not directly correlated with the standard procedure, and the interpretive criteria presently used are too complex for general use. Further analysis indicated that this procedure would not be feasible as a replacement for the standard Bauer-Kirby procedure.

Publications:

None

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01-CL-10049-02 CP |

PERIOD COVERED
October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Evaluation of a New Procedure for Identification of *Enterobacteriaceae*

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Dr. Frank G. Witebsky, Asst. Chief, Microbiology Service, CPD, CC

OTHER: Dr. James D. MacLowry, Chief, Microbiology Service, CPD, CC

COOPERATING UNITS (if any)
None

LAB/BRANCH
Clinical Pathology Department

SECTION
Microbiology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.1 | 0.1 | 0 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Gram negative rods belonging to the genus *Enterobacteriaceae* are among the most common human pathogens. Even with the use of new miniaturized systems, their identification continues to take up a considerable amount of laboratory time and resources. Using microtitration plates prepared in-house with commercially available media, we explored the feasibility of such plates for organism identification, with the goal of determining whether such a procedure can be made adequately accurate, yet less costly than other currently available procedures.

PHS-
(Rev.

Project No. Z01-CL-10049-02 CP

1. Clinical Center, Clinical Pathology Department
2. Microbiology Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Previous Project No.: None

Project Title: Evaluation of a New Procedure for Identification of Enterobacteriaceae

Previous Serial Number: Z01 CL 10049 01

Principal Investigator: Dr. Frank G. Witebsky
Other Investigator: Dr. James D. MacLowry

Man Years:
Total: 0.1
Professional: 0.1
Other: 0

## Project Description

### Objectives:

The objective of this study was the evaluation of media commercially prepared by the Dynatech Corporation for identification of organisms belonging to the genus Enterobacteriaceae, which includes many common human pathogens. We investigated whether a procedure could be devised, and a set of biochemicals selected, so that adequate accuracy of species identification could be attained at a cost less than that of currently available miniaturized systems.

### Methods Employed:

Using the Dynatech MIC2000 96 channel dispenser and media prepared by Dynatech, plates containing selected biochemicals were prepared in-house. The cost and accuracy of this system was compared with that of the API20E system currently used in our laboratory.

### Major Findings:

The project has concluded. Preliminary analysis suggested the feasibility of this system for the identification of certain Gram-negative rods.

However, with the current commercial availability of prepared plates for the same purpose, further work in this area does not appear justified at present.

Publications:

None

| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 10050-02 CP |
|---|---|---|

PERIOD COVERED
October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)
Interactions of Cold Insoluble Globulin with Coagulation Proteins

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: Dr. Craig M. Kessler Staff, Hematology Service, CP CC

COOPERATING UNITS (if any)

BRANCH
Clinical Pathology Department

SECTION
Hematology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1.0 | 0.5 | 0.5 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Cold insoluble globulins (CIg), also known as fibronectin, is a major glycoprotein of vertebrate blood and organ stroma. Fibroblasts and endothelial cells in cell culture synthesize CIg and may act as the sources of circulating CIg in vivo. CIg apparently interacts with platelets, fibrinogen and coagulation factor XIII in vitro; however, its physiologic significance and function have not been established. Many of the existing methods to isolate CIg for study were inadequate. An efficient technique has been examined to purify CIg in large quantities and to render it free of contaminating coagulation proteins and inhibitors. This technique will also provide a means to analyze the interactions between purified coagulation proteins and CIg.

PHS-6040

Project No. Z01 CL 10050 02 CP

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Interactions of Cold Insoluble Globulin with Coagulation Proteins

Previous Project Number: Z01 CL 10050 01 CP

Principal Investigator: Craig M. Kessler, M.D.

Man Years:

| | |
|---|---|
| Total | 1.0 |
| Professional: | 0.5 |
| Other: | 0.5 |

## Project Description

### Objectives:

1. Purification of CIg which is structurally and functionally intact and free of contaminating proteins, which participate in coagulation.

2. Development of an *in vitro* assay of CIg function based on its interaction with coagulation proteins.

3. Examination of CIg as a mediator of platelet aggregation, coagulation protein activation and post-ribosome coagulation protein assembly.

4. Examine the proteolytic fragmentation of CIg by trypsin, plasmin and thrombin. This will provide information regarding molecular structure and may provide a kinetic toll for comparing structures of cell surface bound CIg with circulating CIg.

### Methods Employed:

CIg is purified by passing fresh human plasma over a gelatin affinity column. Proteolytic fragmentation is examined by following changes in pH during digestion of CIg and then calculating the number of bonds cleaved. Sequential samples are examined on SDS-polyacrylamide gel electrophoresis.

### Honors and Awards:

None

Publications:

1. Kessler, C.M., Bell, W.R.: Regulation of Fibrinogen Biosynthesis: Effect of Fibrin Degradation Products, Low-Molecular-Weight-Peptides of Fibrinogenolysis and Fibrinopeptides A and B. J. Lab. Clin. Med. 93: 758-767, 1979.

2. Kessler, C.M., Bell, W.R.: The Effect of Homologous Thrombin and Fibrinogen Degradation Products on Fibrinogen Synthesis in Rabbits. J. Lab. Clin. Med. 93:768-782, 1979.

3. Kessler, C.M., Bell, W.R.: Stimulation of Fibrinogen Synthesis: a possible functional role of fibrinogen degradation products. Blood 55:40-47, 1980.

Presentations:

1. Untreated Thrombocythemia in Chronic Myeloproliferative Diseases. 22nd annual meeting of the American Society of Hematology, December 1979, Phoenix, Arizona.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL-10051-02 CP |

PERIOD COVERED
October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Platelet Membrane Potential Changes

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Dr. Jerome A. Donlon | Staff, Hematology Service, CP | CC |
| Other: | Dr. Bruce Seligman | Research Fellow, LCI, | NIAID |

COOPERATING UNITS (if any)
Laboratory of Clinical Investigation, NIAID

LAB/BRANCH
Clinical Pathology Department

SECTION
Hematology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.05 | 0.05 | |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Fluorescenated cyanine dyes when localized in biological membranes will fluoresce in response to a transmembrane electrical potential change. Recently researchers have demonstrated that the membrane potential of human platelets change in response to stimuli such as ADP and thrombin. Our current project is exploring the basics of this technique and the possibility of using this technique to assess platelet function through clinically relevant responses to various physiological and pharmacological stimuli. Basic questions relating to the mechanism of action of these various agents may also be answered.

PHS-6040
(Rev. 10-76)

Project No. Zol CL-10051-02

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Platelet Membrane Potential Changes

Previous Project No.: Z01 CL-10051-01

Principal Investigator: Dr. Jerome A. Donlon

Other Investigator: Dr. Bruce Seligman

Man Years:

| | |
|---|---|
| Total | 0.05 |
| Professional: | 0.05 |
| Other: | |

## Project Description

### Objectives:

1. Determine optimal preparation and suspension conditions for platelets to give reproducible responses to ADP, thrombin and epinephrine.

2. Evaluate platelet membrane potential response in the presence of various agents (e.g., aspirin, persantin, urea, platelet antibodies, fibrinogen, factor VIII).

3. Evaluate platelet membrane response of abnormally functioning platelets. (Bernard Soulier, storage pool disease).

4. Correlate membrane potential changes with aggregation phenomena or release phenomena. Role of calcium and phospholipids.

### Methods Employed:

Human platelets prepared by low speed centrifugation or gel filtration. Fluoresceinated cyanine dye, measured by a fluorescence spectrophotometer.

### Major Findings:

Discussion with other researchers using this procedure indicates the need for a clean but gentle preparation of platelets (gel filtration recommended), the use of Tyrode's buffer and control of pH by use of $CO_2$ stream. Platelet concentrations should be about 56,000/µl. The concentration of dye used should be on the plateau of the relative fluorescence curve. The potential calibration must be linear and stable when potassium and valinomycin are used.

## Significance to Biomedical Research and to the Program of the Department:

Optimal platelet preparation procedures, buffers and cations for reproducible, meaningful responses will be determined. Membrane response to aggregating agents, antibodies, coagulation factors, aspirin and drugs will be evaluated.

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| MITHSONIAN SCIENCE INFORMATION EXCHANGE<br>PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>**NOTICE OF**<br>**INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br><br>Z01 CL-10052-02 CP |

PERIOD COVERED
October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Platelet Membrane Glycoprotein Study

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | Dr. Jerome A. Donlon | Staff, Hematology Service, CP | CC |
| Other: | Dr. Harvey R. Gralnick | Chief, Hematology Service, CP | CC |

RATING UNITS (if any)

LAB/BRANCH
Clinical Pathology Department

SECTION
Hematology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.05 | 0.03 | 0.02 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

At least three major glycoproteins of human platelet membranes have been defined, purified and characterized. One glycoprotein (GPI) which is absent from the surface of Bernard-Soulier platelets also may be associated with the ristocetin receptor. Our current project proposes to purify sufficient quantities of each of these glycoproteins to allow immuniziation of rabbits or goats and thereby obtain specific antiserum for each glycoprotein. These antisera would then be used to evaluate the presence of each glycoprotein on platelets from patients with thrombosis or bleeding problems. In addition, the antisera can be used to probe the receptor function of each glycoprotein. The study will prepare glycoproteins from the platelets of normal human volunteer donors.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL-10052-02

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Platelet Membrane Glycoprotein Study

Previous Project No.: Z01 CL-10052-01

Principal Investigator: Dr. Jerome A. Donlon

Other Investigators: Dr. Harvey R. Gralnick

Man Years:

| | |
|---|---|
| Total | 0.05 |
| Professional: | 0.03 |
| Other: | 0.02 |

## Project Description

Objectives:

1. Prepare significant quantities of normal human platelet membrane glycoproteins.

2. Obtain specific antiserum to each of the purified glycoproteins.

Methods Employed:

1. Preparation of washed intact platelets by repeated low speed centrifugation.

2. Preparation of platelet membranes by osmotic lysis and ultracentrifugation.

3. Detergent or 3M salt extraction of membrane glycoproteins.

4. SDS-polyacrylamide gel electrophoresis.

5. Column chromatographic separation by molecular weight.

6. Alternatively, lectin affinity chromatography.

7. Standard immunization procedures with purified GP and appropriate IgG isolation and absorption.

## Major Findings:

A prototype run using the platelets from 30 ml of whole blood demonstrates the three GP bands on SDS polyacrylamide gel electrophoresis. This amount of material is insufficient for immunizations, although representing a good yield from the original platelets. Immunization of rabbits has proceeded with human platelets and platelet membrane preparations.

## Significance to Biomedical Research and to the Program of the Department:

1. Extend the preparation to platelet concentrates representing platelets from 500 to 1000 ml of whole blood.

2. Explore various solubilization procedures and detergents, to selectively elute glycoproteins (e.g., preparations that are used to isolate HL-A antigens).

3. Use various lectin affinity columns to minimize preparation time and handling and to selectively isolate glycoproteins.

## Honors and Awards:

None

## Publications:

None

NOTICE OF
INTRAMURAL RESEARCH PROJECT    Z01 CL-10053-02 CP

PERIOD COVERED
October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)
Determination of lactate dehydrogenase isoenzymes for the detection of myocardial infarction in medical and surgical patients.

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

1) Dr. N.M. Papadopoulos, CC, CPD, Research Biochemist, Principle Investigator

2) Dr. W. Z. Borer

3) Dr. R. Michalik, Thoracic Surgeon, NHBLI

COOPERATING UNITS (if any)

LAB/BRANCH
Clinical Pathology Department

SECTION
Clinical Chemistry Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, MD 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.6 | 0.4 | 0.2 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS    ☒ (b) HUMAN TISSUES    ☐ (c) NEITHER

☐ (a1) MINORS    ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The method for the determination of lactate dehydrogenase (LD) isoenzymes and estimation of the ratio of the cardiac specific LD isoenzymes one and two has been improved and applied to the analysis of serum samples from patients for the detection and differential diagnosis of myocardial infarction (MI). General medical patients have been studied as well as patients undergoing heart operations. The improved reliability and diagnostic discrimination of the LD isoenzyme test has provided valuable diagnostic information in the detection of MI and other complications in these patients.

Project No. Z01 CL 10053-02 CP
1. Clinical Pathology Department
2. Clinical Chemistry Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Determination of lactate dehydrogenase isoenzymes for the detection of myocardial infarction in medical and surgical patients.

Previous Serial No.: Z01 CL-10053-01

Principal Investigator: Dr. Nicholas M. Papadopoulos

Other Investigators: Dr. W.Z. Borer and Dr. R. Michalik

| | | |
|---|---|---|
| Man Years: | Total: | 0.6 |
| | Professional: | 0.4 |
| | Other: | 0.2 |

## Project Description

### Objectives:

To improve health care service by providing accurate lab data and interpretation of test results.

1) By improving the reliability of the electrophoretic method for the determination of LD-isoenzymes.

2) By application of the method in clinical studies and association of the test results with the clinical conditions of patients.

### Method Employed:

Electrophoretic fractionation of LD-isoenzymes. Quantitative determination by densitometry. Estimation of the ratio LD-1/LD-2.

### Major Findings:

1) Accurate determination of LD-isoenzymes has provided valuable information for the differential diagnosis of MI in patients with various medical complications as illustrated in a recent case report (1).

2) Determination of LD-isoenzymes and estimation of the ratio LD-1/LD-2. has been established as a useful biochemical index for the diagnosis of MI in patients undergoing cardiac operations.

### Significance to Biomedical Research and the Program of the Institute:

Clinical applications of the LD-isoenzyme test provided useful information for the interpretation of test results and their association with the clinical events; specifically the diagnosis of MI in medical and surgical patients.

### Proposed Course:

Application of the test to the analysis of serum samples from the unique NIH patient population:

a) To provide information which aids the diagnosis of disease and follow up of therapy and

b) To gain new information for the advancement of biomedical knowledge.

### Publication:

1) Borer, W.Z., Gottdiener, J.S. and Papadopoulos, N.M.: Myocardial infarction a conflict between EKG changes and biochemical data. Clin. Chem., 25, 1853, 1979.

[illegible] PROJECT | Z01 CL-10054-02 CP

[illegible]

October 1, 1979 through September 30, 1980

TITLE OF PROJECT [illegible]

Electrophoretic Determination of Serum Lipoproteins, in Normal Subjects and Patients

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Dr. N.M. Papadopoulos, Research Biochemist, Principle Investigator

COOPERATING UNITS (if any)

LAB/BRANCH

Clinical Pathology Department

SECTION

Clinical Chemistry Service

INSTITUTE AND LOCATION

CC, NIH, Bethesda, MD 20205

| | | |
|---|---|---|
| TOTAL MANYEARS:<br>0.55 | PROFESSIONAL:<br>0.25 | OTHER:<br>0.3 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The agarose gel electrophoretic system for the determination of lipoproteins has been improved and applied in the study of serum samples from normal subjects and patients with dyslipidemias. Abnormal lipoprotein patterns characterized by the absence of lipoprotein fractions and by the presence of extra fractions have been demonstrated and associated with defined pathological conditions. All these patterns form a reference record for the diagnosis and evaluation of lipoprotein abnormalities in normal subjects and patients. In addition an abnormal lipoprotein has been demonstrated in the serum of uremic patients which may be associated with accelerated atherosclerosis.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10054-02 CP
1. Clinical Pathology Department
2. Clinical Chemistry Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Electrophoretic Determination of Serum Lipoproteins, in Normal Subjects and Patients

Previous Serial No.: Z01 CL-10054-01

Principal Investigator: Dr. Nicholas M. Papadopoulos

Other Investigator: Mr. D. Everett

| Man Years: | | |
|---|---|---|
| | Total: | 0.55 |
| | Professional: | 0.25 |
| | Other: | 0.3 |

## Project Description

**Objectives:**

To enhance the accuracy of lab tests and the clinical usefullness of test results for the purpose of improving health care lab service.

1) By improving the electrophoretic method used for the determination of serum lipoproteins.

2) By application of the method in clinical investigations to study changes of normal lipoprotein electrophoretic patterns associated with defined pathological conditions. This forms the basis for the interpretation of test results and their association with clinical conditions.

**Methods Employed:**

Fractionation of serum lipoproteins by agarose gel electrophoresis; application of the test for the determination of lipoprotein patterns in normal subjects and patients with various pathological conditions.

**Major Findings:**

The application of the improved agarose gel electrophoretic system for the determination of lipoproteins in serum samples from normal subjects and patients resulted in the following new information:

1) Update and expansion of the lipoprotein phenotyping system.

2) Determination of abnormal lipoprotein patterns in the serum of patients and their association with defined pathological conditions. All these patterns form a reference record for the diagnosis and evaluation of lipoprotein abnormalities in normal subjects and patients. They provide useful information for appropriate treatment with established therapeutic measures. Basic information on the association of lipid abnormalities with atherosclerotic cardiovascular disease.

**Significance to Biomedical Research and the Program of the Institute:**

The detection of lipoprotein abnormalities aids the early intervention by therapeutic measures for the prevention of atherosclerotic cardiovascular diseases. The sensitive electrophoretic test system employed accomplishes this purpose. In addition, the detection of abnormal lipoprotein fractions in the serum of patients with accelerated atherosclerosis aids the understanding of the role of lipoprotein on the atherosclerotic process.

Proposed Course:

Continued application of the lipoprotein electrophoretic test system for the following purposes:

1) To detect lipoprotein abnormalities characterized by the presence of extra lipoprotein bands or the absence of lipoprotein fractions in serum, and their association with clinical conditions.

2) The study of the role of lipoproteins in the pathogenesis of atherosclerosis.

Publications:

1) Papadopoulos, N.: Abnormal lipoprotein patterns in human serum as determined by agarose gel electrophoresis. Clin. Chem. 25, 1885, 1979.

2) Papadopoulos, N., Borer, W.Z., Elin, R.J., and Diamond, L.H.: An abnormal lipoprotein in the serum of uremic patients. Ann. Int. Med. 92, 634, 1980.

| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER |
|---|---|---|
| | | Z01 CL 10055-01 CP |

PERIOD COVERED

October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Evaluation of Platelet Factor 4 and β Thromboglobulin Assays.

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | |
|---|---|---|
| PI: | Dr. Jerome A. Donlon | Staff, Hematology Service, CPD, CC |
| Other: | Dr. Harvey R. Gralnick | Chief, Hematology Service, CPD, CC |

COOPERATING UNITS (if any)

LAB/BRANCH

Clinical Pathology Department

SECTION

Hematology Service

INSTITUTE AND LOCATION

CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.20 | 0.20 | 0.0 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Platelet factor 4 and β thromboglobulin are proteins contained in the alpha granules of platelets. They are released upon platelet activation. Elevated levels of these proteins in the plasma of some patients may indicate a predisposition to or ongoing thrombosis.

A radioimmunoassay kit for platelet factor 4 was evaluated for sensitivity, specificity, precision, accuracy and reproducibility. The assay performed to the specifications indicated. The most critical aspect was the collection of appropriate specimens. Various anticoagulant and anti-aggregation agents were evaluated as well as a one- versus two-syringe blood drawing technique. The optimal specimen is obtained by an atraumatic venipuncture using a two-syringe collection into an EDTA-citrate-theophylline-$PGE_1$ anticoagulant/anti-aggregant buffer.

A radioimmunoassay kit for β thromboglobulin was evaluated for sensitivity, specificity, precision, accuracy and reproducibility. These parameters were found to be satisfactory. Specimens collected as above but using a collection tube with anticoagulant/anti-aggregant buffer supplied with the kit were satisfactory.

An evaluation of normal ranges for males and females is currently in progress.

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Evaluation of Platelet Factor 4 and β Thromboglobulin Assays.
Previous Project No.: None
Principal Investigator: Dr. Jerome A. Donlon

Other Investigator: Dr. Harvey R. Gralnick

Man Years:

| | |
|---|---|
| Total: | 0.20 |
| Professional: | 0.20 |
| Other: | 0.00 |

## Project Description

### Objectives:

1. Evaluate radioimmunoassay kit for assay of platelet factor 4.

2. Evaluate radioimmunoassay kit for assay of β thromboglobulin.

3. Determine appropriate specimen collection technique, specimen handling and anticoagulants and/or anti-aggregants.

4. Determine range of values in normal male and female donors.

### Methods Employed:

Specimen collection by two-syringe technique and butterfly needle.

Specimen preparation by centrifugation and aliquoting 0.5 ml of plasma.

Radioimmunoassay using I-125 labelled tracer proteins and specific antisera as supplied in kits.

### Major Findings:

Inappropriate specimen collection or handling will cause spurious elevations in platelet factor 4 and β thromboglobulin levels. Careful specimen collection through atraumatic venipuncture and two-syringe collection into appropriate anticoagulant/anti-aggregant buffer is essential.

Theophylline and $PGE_1$ are appropriate anti-aggregants, however, theophylline alone may suffice. EDTA and citrate are appropriate anticoagulants, a combination of both may be preferred.

Major Findings (continued):

The assays performed to specifications with good sensitivity, accuracy, precision and reproducibility. Recovery tests and dilutions for linearity were acceptable. There was no cross-over interaction between the platelet factor 4 and β thromboglobulin antisera specificity.

Significance to Biomedical Research and to the Program of the Department:

1. These assays will be useful in clinical evaluation of thrombosis or prethrombosis states.

2. Clinical data will be collected in association with other tests for thrombosis evaluation.

3. These assays are useful in research experiments which require an evaluation of platelet activation or release.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE
PROJECT NUMBER (Do **NOT** use this space)

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
**NOTICE OF**
**INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 CL 10056 -01 CP

PERIOD COVERED

October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Evaluation of Fluorogenic Substrate Assays for Heparin, Antithrombin III, Plasmin and Plasminogen

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | |
|---|---|---|
| PI: | Dr. Jerome A. Donlon | Staff, Hematology Service, CPD, CC |
| Other: | Dr. Harvey R. Gralnick | Chief, Hematology Service, CPD, CC |

COOPERATING UNITS (if any)

LAB/BRANCH
Clinical Pathology Department

SECTION
Hematology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.20 | 0.15 | 0.05 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

A field trial of commercially available fluorogenic substrate reagent kits and dedicated fluorometer was undertaken to evaluate this system's appropriateness to our research and clinical care efforts. Synthetic substrate for proteolytic enzymes can be made. The substrates are then tagged with a chromogenic or fluorogenic group such that after cleavage of the substrate the active group is released and becomes chromatically active or fluorescent. The rate of release of the group is proportional to enzyme concentration in a substrate excess assay. Many coagulation or fibrinolytic enzymes are proteolytic. Of particular interest are thrombin and plasmin. Assays for heparin and antithrombin III can be generated by adjusting reagents such that they are the rate-limiting factors in generation of thrombin.

The current results of our evaluation showed a drift and variability in the baseline zero for heparin and antithrombin III which was determined to be unacceptable. The accuracy and precision was also not clinically acceptable. Adjustments in the substrate-reagents mixture or the instrument electronics may be necessary to correct these deficiencies. The plasminogen, plasmin assays were only briefly evaluated but appear promising as rapid, stable, reliable assays.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10056-01 CP

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Evaluation of Fluorogenic Substrate Assays for Heparin, Antithrombin III, Plasmin and Plasminogen

Previous Project No.: None

Principal Investigator: Dr. Jerome A. Donlon

Other Investigator: Dr. Harvey R. Gralnick

Man Years:

| | |
|---|---|
| Total: | 0.20 |
| Professional: | 0.15 |
| Other: | 0.05 |

## Project Description

### Objectives:

1. Determine the precision, accuracy, sensitivity and linearity of fluorogenic substrate assays for heparin, antithrombin III, plasminogen and plasmin.

2. Compare results of fluorogenic substrate assays to results of assays currently in use in our laboratory for antithrombin III, plasmin and plasminogen.

3. Compare the results of the fluorogenic substrate assay for heparin to activated partial thromboplastin time (APTT) assays.

4. Evaluate the overall suitability of utilizing these assays in our clinical service.

### Methods Employed:

Commercially available fluorogenic substrate assay kits were used to assay standards, controls, blanks and selected donor plasmas for heparin, antithrombin III, plasmin or plasminogen. These assay results were determined using a dedicated commerical fluorometer provided by the same company which manufactures the reagent kits. APTT, casein hydrolysis and Mancini RID were also used for comparative results.

### Major Findings:

It was difficult to maintain a stable day-to-day zero baseline when the heparin or antithrombin III assays were performed. This necessitated daily baseline adjustments. Duplicate assays showed poor linear agreement.

Major Findings: (continued)

Standard curves (5 determinations per point) were linear but on a day-to-day comparison were not reproducible. These assays were judged not currently acceptable.

Projection:

1. The company is re-evaluating their reagents and instrumentation to correct the above defects if possible.

2. A reliable assay for heparin levels would be clinically useful.

3. We will evaluate similar tests which utilize chromogenic substrates and spectrophotometers.

4. A more complete evaluation of the plasmin and plasminogen kits will be done.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 10057-01 CP |

PERIOD COVERED
October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Studies of Patients with Inhibitors of Blood Coagulation

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | |
|---|---|---|
| PI: | Dr. Richard N. Palmer | Staff, Hematology Service, CPD, CC |
| Others: | Dr. Margaret Rick | Staff, Hematology Service, CPD, CC |
| | Dr. Harvey Gralnick | Chief, Hematology Service, CPD, CC |

COOPERATING UNITS (if any)

LAB/BRANCH
Clinical Pathology Department

SECTION
Hematology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.5 | 0.5 | 0 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Two patients with inhibitors of blood coagulation have been identified, and their inhibitors have been characterized in preliminary studies. One appears to have a heparin-like inhibitor. The other is an IgM lupus-like inhibitor which inhibits factor VIII coagulant activity.

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10057-01 CP

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Studies of Patients with Inihibitors of Blood Coagulation

Previous Project No.: None

Principal Investigator: Dr. Richard N. Palmer

Other Investigators: Dr. Margaret Rick
Dr. Harvey Gralnick

Man Years:

| | |
|---|---|
| Total: | 0.5 |
| Professional: | 0.5 |
| Other: | 0.0 |

## Project Description

### Objectives:

To elucidate the biochemical characteristics and molecular interactions of the above-mentioned inhibitors.

### Methods Employed:

Established techniques of biochemistry, immunology and coagulation are being utilized. These include ion exchange, gel filtration and affinity chromatography, immunodiffusion and immunoelectrophoresis and clotting factor assays.

### Major Findings:

Preliminary findings indicate these are two different inhibitors in terms of both biochemical characteristics and mode of action. One is heparin-like in action and appears to have an $M_R$ of 100,000-200,000 daltons. The other is an anti-factor VIII anti-prothrombinase and has characteristics of IgM.

### Significance to Biomedical Research and the Program of the Department:

Identification of the mechanism of action of these inhibitors will allow decisions regarding the necessity of treatment and the type of treatment to be employed in these types of individuals. It will also help in understanding the role of heparin-like inhibitors in normal hemostasis and thrombosis.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE
PROJECT NUMBER (Do NOT use this space)

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
**NOTICE OF**
**INTRAMURAL RESEARCH PROJECT**

PROJECT NUMBER

Z01 CL 10058-01 CP

PERIOD COVERED
October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Investigation of Variants of von Willebrand's Disease

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | |
|---|---|---|
| PI: | Dr. Margaret E. Rick | Staff, Hematology Service, CPD, CC |
| Other: | Dr. Harvey R. Gralnick | Chief, Hematology Service, CPD, CC |

COOPERATING UNITS (if any)

LAB/BRANCH
Clinical Pathology Department

SECTION
Hematology Service

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.4 | 0.1 | 0.3 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Plasma from patients with von Willebrand's disease are being studied to characterize their content of factor VIII components.

PHS-6040
(Rev. 10-76)

Project No.
Z01 CL 10058-01 CP

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Investigation of Variants of von Willebrand's Disease
Previous Project No.: None
Principal Investigator: Dr. Margaret E. Rick

Other Investigator: Dr. Harvey R. Gralnick

Man Years:

| | |
|---|---|
| Total: | 0.4 |
| Professional: | 0.1 |
| Other: | 0.3 |

## Project Description

### Objectives:

To understand the factor VIII components in patients with variants of von Willebrand's disease.

### Methods Employed:

Laurell immunoelectrophoresis, crossed immunoelectrophoresis, radioimmunoassays for factor VIII related antigen and factor VIII coagulant antigen and coagulation assays are utilized in these studies.

### Major Findings:

Preliminary data indicate a good correlation of factor VIII coagulant and factor VIII coagulant antigen in these patients.

### Significance to Biomedical Research and the Program of the Department:

This group of patients has not been previously fully characterized by these techniques. It is hoped that this will allow a better understanding and possibly a better classification of this group of patients.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE<br>**NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01-CL-10059-01 CP |

PERIOD COVERED
October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Comparative Evaluation of Gentamicin Serum Assays

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI: Dr. Frank Witebsky, Asst. Chief, Microbiology Service, CPD, CC

Other: Dr. James D. MacLowry, Chief, Microbiology Service, CPD, CC
Sally T. Selepak, Technologist, Microbiology Service, CPD, CC

COOPERATING UNITS (if any)

None

LAB/BRANCH
Clinical Pathology Department

SECTION
Microbiology Service

INSTITUTE AND LOCATION
Clinical Center, Naional Institutes of Health, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS:<br>0.4 | PROFESSIONAL:<br>0.1 | OTHER:<br>0 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☒ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Accurate, rapid measurement of serum gentamicin levels is critical for optimal patient care because of the low toxic-therapeutic ratio of gentamicin and the consequent need to make dosage adjustments quickly. In this study, a bio-assay, fluorescent immunoassay, an enzyme immunoassay, a radio-immunoassay, and a latex agglutination inhibition test were compared for their utility in measuring serum gentamicin levels in a clinical setting.

PHS-6040
(Rev. 10-76)

Project No. Z01-CL-10059-01-CP
1. Clinical Pathology Dept.
2. Microbiology Service
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Comparative Evaluation of Gentamicin Serum Assays

Previous Serial No.: Z01-CL-10050-01

Principal Investigator: Dr. Frank G. Witebsky
Other Investigator: Dr. James D. MacLowry
Sally T. Selepak
Cooperating Units: None

Man Years: Total 0.4
Professional 0.1
Other 0

## Project Description

### Objectives:

The objective of this study was the comparison of a variety of methods for measuring serum gentamicin levels in order to select the optimal procedure for our laboratory.

### Methods Employed:

Four commercially-available assay procedures (enzyme immunoassay, radioimmunoassay, fluorescent immunoassay, and latex agglutination inhibition) were compared with one another and with the standard disc-diffusion bioassay. Residual material from patient samples and serum to which known amounts of gentamicin had been added were assayed by the different techniques to assess their accuracy and reproducibility. A variety of statistical techniques are being employed to analyze the data which has been obtained.

### Major Findings:

The data are currently being analyzed statistically. It became clear early in the course of the study that, because of its speed, accuracy, and relative simplicity, the enzyme immunoassay procedure was the optimal one for our institution.

## Significance:

The results of this investigation should provide data useful to other institutions for helping them select an appropriate gentamicin assay procedure for their needs. They have already enabled us to select a new procedure for our institution.

## Proposed Course:

After completion of the data analysis, the results will be published.

## Publications:

None

|  |  |  |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>**NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 10060 01 |

PERIOD COVERED

October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

Determination of Reference Ranges for the Clinical Pathology Department Using NIH Employees

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Principal Investigator: Dr. Ronald J. Elin

Other Investigators:
Dr. Harvey Gralnick
Dr. Sharon McClean
Dr. E. Arthur Robertson

COOPERATING UNITS (if any)

None

LAB/BRANCH

Clinical Pathology Department

SECTION

Clinical Chemistry Service

INSTITUTE AND LOCATION

CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.5 | 0.25 | 0.25 |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

PHS-6040
(Rev. 10-76)

Project No. Z01 CL 10060-01 CP

PHS-NIH
Individual Project Report
October 1, 1979 through September 30, 1980

Project Title: Determination of Reference Ranges For The Clinical Pathology Department Using NIH Employees

Previous Serial No.: None

Principal Investigator: Dr. Ronald J. Elin

| | | |
|---|---|---|
| Man Years: | Total | 0.5 |
| | Professional | 0.25 |
| | Other | 0.25 |

## Project Description

**Objectives:**

To determine accurate reference ranges for many analytes offered by the Clinical Pathology Department.

**Methods Employed:**

A blood specimen will be obtained from approximately 1200 NIH employees in a basal state and tested for a variety of analytes. Each employee completes a five page questionnaire which includes factors of diet, health habits, exercise, etc. Five blood samples will be obtained from each employee at 6 month intervals. The duration of the study which began in July, 1980 will be 2 1/2 years.

**Major Findings:** None

October 1, 1979 through September 30, 1980

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

DIAGNOSTIC RADIOLOGY DEPARTMENT

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October 1, 1979 through September 30, 1980

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

# SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
# CLINICAL CENTER

## DIAGNOSTIC RADIOLOGY DEPARTMENT

### DEPARTMENTAL MISSIONS AND GOALS

The primary raison d' etre of the DRD is the provision of the highest quality and most comprehensive diagnostic radiologic service to the patients in the Clinical Center. We have been able to meet our obligations in this regard during the past year in spite of the impact of major departmental renovations. The delivery of quality radiographic service requires that we attract and retain professionals of unusual medical competence and that we make major efforts to remain in the forefront of diagnosis. These latter efforts demand not only the inhouse development of new diagnostic techniques but the rapid adoption of worthwhile techniques developed elsewhere. Particularly dependent upon recent technological advances in electronic and imaging technology, the DRD has been able to recruit the enthusiastic support of the Clinical Center administration in assuring that its major diagnostic equipment is "state-of-the-art".

During the past year we have assumed an increasingly important and active educational function. There have been further improvements in our inhouse teaching conferences which permit us to meet with the CC medical staff for individualized discussion of patient problems and for instruction in the indications for, the interpretation of, the complications of, and the contraindications to various x-ray studies. As radiologists become increasingly able to make diagnostic and therapeutic contributions to patient care, it has become ever more important that the clinician be instructed in the opportunities afforded by the use of these techniques.

Department sponsorship of a bimonthly areawide computered tomography (CT) meeting developed from our recognition that we ought play a more active role in the local radiologic community. During the past year we sponsored four such meetings which were very enthusiastically received by the participating radiologists from the Baltimore-Washington area. CME credit for the CT meeting has been approved. As an additional offshoot of NIH expertise in CT, a one week course in computed tomographic and ultrasonic techniques has been offered and has been extremely well received by the local radiologists in attendance.

There has historically been a peculiar dichotomy in the direction of Clinical Center service departments with regard to research. An attempt is made to optimize patient care and simultaneously to foster an academic and research environment. Careful personnel selection and utilization are required to allow the harmonious co-existence of these two functions which can at times be antagonistic. However, in discussion between this and other patient care

departments it has been possible for us in many instances to develop and rapidly incorporate new techniques into our armamentarium which techniques have been responsive to the needs of the clinical care physicians. Intra-departmental basic research and inter-departmental clinical research projects in several areas have permitted significant improvement in the delivery of patient care.

Continuing efforts to improve the overall efficiency of our radiographic diagnostic functions and the improvement of departmental responsiveness to changing Clinical Center needs have met with some success. The use of inter-departmental teaching conferences, the Clinical Center department heads meeting, and the Medical Board as forums to explain our ability or inability to meet all Clinical Center needs has proven very helpful.

One of the major goals of the Department during this past year (a goal which will remain a major one until the completion of the ACRF) has been to minimize the disruption of services caused by major departmental renovations and simultaneously to plan for the smooth and expeditious transfer of function into the new department in the ACRF. However, in addition to meeting the immediate and predictable needs for patient care the new facility has been designed in such a way so as to encourage maximal flexibility and so as to permit the future installation in the Department of diagnostic equipment which may be developed within the next two or three decades.

DEPARTMENTAL ACTIVITIES

Despite the disruptive impact upon the Department of major renovations (removal and replacement of the Special Procedures equipment and of the EMI 1010 CT scanner, the absence of the Chief on sabbatical, and the devotion of many hours of effort to the planning of the ACRF) I am able to report that our productivity increased in most areas. As has been true in the past several years, an increase in both the number of conventional x-ray examinations and the total number of diagnostic examinations has been observed, (the increases in these areas are 4% and 3% respectively). Concomitant with this increase has been an active effort by the Department to decrease the numbers of routine examinations obtained in previous years (i.e., routine admission chests and annual physical examination chests) and to be more selective in obtaining x-rays on patients (i.e., discontinuance of routine metastatic series on NCI patients). Thus, in spite of the fact that we have discontinued many examinations in an attempt more rationally to control x-ray diagnostic procedures, to minimize costs, and to control low level radiation exposure to the population, we have nonetheless seen an increase in the numbers of studies performed by the Department.

Modest numerical increases were observed in Special Procedures and in CT in spite of the fact that major renovations in the Special Procedures and CT suites deprived us of optimal equipment for the performance of these examinations. Special Procedures were performed for a period of 3 months on an elderly unit which was also used for the daily fluoroscopic schedule, and head CT examinations were performed on a unit 6 floors removed from the Department. The professional and technical staff of this Department deserve very special kudos for their hard work and dedication during what was a trying period whi

could have been a catastrophe without their efforts. I note with some pride that despite these difficulties the numbers of special examinations increased by 7% as compared to last year and the number of CT body scans increased by 14% (see table of Department Activities, DR-9).

## Computed Tomography

Physician acceptance of CT scanning techniques has continued to be very enthusiastic and as a result of the increased demand for scans and the changing ratio of head/body scans (in fiscal year 1980 1/.8 and in fiscal year 1981 1/1.1) we felt it essential to modernize and improve our scanning capacity. We were able to secure the cooperation of the Clinical Center Administration in this modernization effort and we placed an order for a GE head scanner (which could with ease and speed be converted to a body scanner if need be) on May 3, 1979. The schedule for procurement and renovations slipped several times during Fall and Winter, but by March 1980 our old head scanner was removed and renovations were commenced. Fortunately, we were able without major difficulty to accommodate almost all needs for head and body CT scans during the period of renovation, and only an anecdotal several patients had to be sent to Suburban Hospital (with whom I had made arrangements for standby emergency scans). Installation of the GE head scanner was complete by the second week in June and as the demand for body scanning capacity (as had been predicted) continued to increase I ordered the immediate updating of the unit to a universal scanner which was completed by the 20th of June. The new scanning facility, which is operating quite satisfactorily, will be further modernized and updated by the installation of the scout view localization device by end-July.

The new CT suite is an attractive and efficient one which we anticipate will permit us to resume active research in the CT area - in this regard we have been severely handicapped by the prolonged downtime and by the fact that the equipment we recently replaced was no longer state-of-the-art. A total of 15 papers based on work with the CT scanners was published by the Department during the past year; however, many of the papers were based on data gathered prior to the beginning of or very early in fiscal year '81.

The fact that we again have state-of-the-art scanning capacity will permit an intensive investigation of pituitary microadenomata, the continuing study of demyelinating diseases, the study of defects in the liver of various storage diseases and hepatic response to therapy, and the development of a dynamic scanning capacity heretofore not possible on the older scanning units.

I have already alluded to the success of the areawide CT conference established by the Department in the past year, and the new installation should permit us to continue to act as a paradigm for the local community. We anticipate increased popularity to the Computed Tomography/Ultrasound course given by the Department.

The images generated by the new GE scanner are, as expected, of superior quality. Therein lies the nidus of a new problem - it will not be possible for us to perform all scans on the GE, and some patients will, of necessity, be scanned on the older EMI unit, the images from which are demonstrably inferior.

The DRD will make the determination as to which patients are scanned on whi unit and will expect the cooperation of the CC staff in this regard. Standby arrangements with Suburban Hospital will be maintained to afford us coverage for head scans during any period of time during which our only head scanner, i.e., the GE, is not operating. The problem of nonavailability of scans due to equipment failure and the disparity in the quality of the scans generated by the two Department units will be resolved only when a second state-of-the-art scanner replaces the now out-of-date EMI body scanner.

The evolution of scanning technology and the high mortality rate among the manufacturers of scanners poses a terrible dilemma for radiologists everywhere in terms of what to order and when. Fortunately, we still have a time lag of 6 to 8 months before we will be required to order the first scanner for the ACRF, and we hope that during that period of time the dust will have settled sufficiently to permit us to make a rational decision.

The two Departmental scanners require two fulltime radiologists, five technicians and one appointment file clerk.

Ultrasound

There has been a slight decrease in the numbers of patients scanned ultrasonographically, but the Ultrasound Section of the Department has been able adequately to meet the patient needs of the Clinical Center. Severely constrained by limitations of space and congestion in the ultrasound examining room, I anticipate that no significant increases in the numbers of studies performed will be possible until the serious space limitations are overcome. It appea that the DRD will not move into the ACRF until 18 to 24 months from now, and, as a consequence, I have decided to proceed with installation of the Stratomatix Multidirectional Planograph in the existing Department so as to permit the Ultrasound Section to expand somewhat. Research activities in this area continue to be extensive and resulted in the past year in the publication of 5 articles, a textbook, presentation at the meeting of the American Academy of Rehabilitation and Physical Medicine, and an exhibit at the meeting of the Radiological Society of North America.

The project mentioned last year for the development of a screening program for the diagnosis of gallbladder disease performed in conjunction with the National Institute of Arthritis, Metabolism and Digestive Diseases and the National Center for Health Statistics has entered Phase II which entails the purchase of equipment and the training of technical staff. Phase III of the study will begin in November and will involve the screening of 15,000 normal volunteers for evidence of gallstones.

Use of the Sonoscope, which was designed and built by the National Bureau of Standards through an NIH grant, resulted in a publication of amplitude analysis of the pancreas during the past year and is currently being used for amplitude analysis of the thyroid in thyroiditis and of the liver in patients with Gaucher's disease.

Increasing clinical usage of the modality for ultrasonically guided aspiration of various pathologic sites has been undertaken and a new project using

this technique for the study of thyroid nodules is being carried out with the cooperation of the Clinical Endocrinology Branch of the NIAMDD. So as to improve the efficiency of ultrasonically guided biopsy and aspiration, the development and construction of an ultrasonic real-time aspiration transducer is being undertaken with the cooperation of the Biomedical Engineering and Instrumentation Branch of the Clinical Center.

An analysis of tongue movement in patients with neurologically impaired speech is being made in cooperation with the Physical Therapy Department of the Clinical Center in hopes of developing a new technique to permit the rehabilitation of such patients.

In a joint study with the CT Section of the DRD and the Surgery Branch of NCI an evaluation of the sensitivity of ultrasound for the detection of liver metastases in patients with cancer of the colon has been begun. Much data has been accumulated in this study and publication of preliminary results is to be expected in the near future.

The Ultrasound Section co-sponsored with the National Bureau of Standards the 5th International Symposium of Ultrasonic Issuing and Tissue Characterization in June 1980. Approximately 400 physicians, physicists, and technicians were in attendance.

The Ultrasound Section has required two fulltime radiologists, two technicians and an appointment file clerk. Maintenance costs in this section approximated $6,000.00 during the course of the year.

## Special X-Ray Procedures

For the past several years there has been an ongoing increase in the number of special x-ray procedures - an increase which was again observed this year. In spite of the absence of the chief of the Department, who is a very active angiographer, the Department performed more special x-ray examinations than ever before in its history. Increasing numbers of these procedures are highly sophisticated and extremely time consuming. Examinations involving multiple selective and superselective vascular catheterizations continue to increase in number and place a disproportionate demand on the technical staff manning this area. In the past year transluminal angioplasty, percutaneous nephrostomy and percutaneous biliary drainage techniques have been incorporated into our therapeutic armamentarium. These three interventional radiographic-therapeutic techniques have in selective instances proven to be of great clinical value and have permitted the postponement and/or cancellation of major surgery in patients in whom the techniques have been applied.

The reorganization of the Neurosurgical Department of the NINCDS has begun to have its anticipated effect on the DRD; i.e., the numbers of cerebral angiograms have increased by about 60% in the past year with most of the increase being in the latter part of the year. New protocols involving the study of pituitary microadenomata and the therapy of unresectable primary tumors of the CNS are expected to cause a continuing and marked increase in the numbers of cerebral angiograms performed. One can note from the chart below that there has been diminution in the numbers of head scans performed - in part because

we felt it necessary to cancel the performance of all head CT studies on patients from Walter Reed, Bethesda Naval, and St. Elizabeth's hospitals. Several years ago almost 50% of the total head scans performed at the Clinical Center were performed on patients from these other federal installations; thus the 2381 head studies performed this year realistically reflect a baseline number of such scans when we service only NIH patients.

| Date | Head CT | Cerebral Angiography | Pneumo-encephalography |
|---|---|---|---|
| 7/1/74 - 6/30/75 | -- | 135 | 52 |
| 7/1/75 - 6/30/76 | 1877 | 94 | 13 |
| 7/1/76 - 6/30/77 | 2750 | 67 | 9 |
| 7/1/77 - 6/30/78 | 2936 | 72 | 6 |
| 7/1/78 - 6/30/79 | 2655 | 32 | 2 |
| 7/1/79 - 6/30/80 | 2381 | 52 | 2 |

I have engaged in ongoing discussions with Clinical Center Administration regarding the performance of head scans in the interim period between now and the occupancy of the ACRF when we will have no backup head scanning capacity (when the GE scanner is out of operation because of routine maintenance or breakdown - expected to be 5-10% of the time). I have made tentative arrangements with Suburban Hospital to perform emergency head scans under these circumstances and I hope to be able to fulfill the legitimate needs of the Clinical Center under all circumstances using this standby coverage arrangement.

During the past year we have replaced the Special Procedures Room - the new installation is now complete and fully operational. A $650,000 Philips Poly-Diagnostic UPI has been installed to replace an outmoded and senescent CGR unit which could no longer adequately be maintained. It should be emphasized that the increase in numbers of special procedures performed by the Department occurred in spite of the fact that for 3 months of the past year we were performing special procedures in a standby fluoroscopic suite which was far from optimal for patients and physicians alike. Extraordinary dedication on the part of the physician and technician staff was required in the effort to maintain responsiveness to Clinical Center needs and adequacy of diagnostic studies.

Research Facility

The number of animal studies performed in the research facility this year remained stable. The ultrasonic study of obstructed common bile ducts and a report on the temporal sequence of events following obstruction and relief of obstruction has been completed and the results have been reported. Studies of contrast media induced injury of the spinal cord with measurements of CSF iodine levels and histologic examination of the spinal cord seriatim after injury are continuing. The evaluation of the topo catheter and balloon catheters, which are fabricated at NIH, in an attempt to improve our ability to

direct catheter tips into vessels heretofore inaccessible continue promising. At the same time that we have incorporated percutaneous angioplasty into our clinical armamentarium we have begun to prepare an animal model for atherosclerosis to permit our assessment of the techniques for and the effects of balloon catheter dilatation of diseased arteries. Animal studies of a technique for opening the blood-brain barrier by the selective infusion of manitol into the internal carotid artery are being studied in hopes of improving the effect of chemotherapy on primary and secondary neoplasms of the brain. Studies of the NIH-developed contrast medium EOE 13 continue with attempts being made to determine optimal particle size for this organ specific contrast medium and to determine the clearance time of the medium from the liver. Using EOE 13 as the contrast medium, angiographic and CT studies of primates with carcinogen induced hematomas are being performed pre- and post-chemotherapeutic attack.

Two fulltime technical personnel work with members of the professional staff to main the research facility.

## Teaching and Education

We remain the most active of all Clinical Center Departments in the numbers of inter-departmental conferences given. In addition to their effect on the optimization of patient care, the conferences act as a bully pulpit from which the radiologists can discuss the latest advances in diagnostic and therapeutic radiologic techniques; in this regard the conferences have proven both very well received and extremely effective. Members of the staff are routinely scheduled to give teaching sessions at DC General Hospital, George Washington University Hospital, AFIP and USUHS. A program for the rotation of third year medical students from USUHS has been developed and these students are rotating through the Department on a regular basis. The chairman of the Department has been appointed as Clinical Professor of Radiology, the Deputy Chief has been appointed Associated Professor of Radiology and the Chief of Ultrasound has been given the title of Assistant Professor of Radiology on the USUHS staff. Several new consultants to the Department from the staffs of the AFIP and USUHS have been named and these physicians have made a valuable contribution to the ongoing professional education of the departmental professional staff. The departmentally sponsored regional CT meeting has been extremely well received and is the best attended of all such after hours radiographic conferences in the area. The CT/US course given by the Department has been regularly attended and we have applicants for attendance through the remainder of the calendar year.

## MAJOR PROJECTS AND RESEARCH

Listed below are the major research projects now under investigation in the Department. The appended description of the projects are adequate and require no summation. (See Project Reports, pp DR-17 - DR-34)

1. IV Hepatosplenography
2. Evaluation of Contrast Agents for Transcatheter Organ Ablation
3. Biodistribution Study of Intravenously Injected Particulate Suspensions

4. Lymphography in Oncologic Patients
5. Ultrasound Analysis of Iron Storage Diseases
6. Ultrasound Analysis of Ovarian Structures in Patients Undergoing Chemotherapy
7. Ultrasound Screening of Asymptomatic Individuals for Chololithiasis
8. Ultrasound Analysis of Diffuse Liver Disease
9. Efficacy of Ultrasound Imaging for Detecting Liver Metastases
10. Real-Time Ultrasound Study of Speech
11. Ultrasound Amplitude Analysis of Diffuse Thyroid Disease and Thyroid Nodules
12. Development of Ultrasound Real-Time Biopsy Transducer
13. Detection of Pulmonary Metastases by Computed Tomography
14. Localization of Functional Adrenal Tumors

## SUMMARY OF DEPARTMENT ACTIVITIES

| | 7/1/78-6/30/79 | 7/1/79-6/30/80 | % Change (79-80) |
|---|---|---|---|
| #MD's | 12-13 | 11.5-13.5 | 0% |
| #Technicians | 24-26 | 28-30 | +13% |
| #Other Staff | 26 | 26 | 0% |
| #X-Ray Exams | 48167 | 50136 | +4% |
| #Department Diagnostic Exams | 56521 | 58454 | +13% |
| #Specials | 869 | 929 | +7% |
| #CT Head | 2655 | 2381 | -10% |
| #CT Body | 2297 | 2615 | +14% |
| #Ultrasound Exams | 1728 | 1601 | -7% |
| #Animal Research Exams | 805 | 792 | -2% |
| #Publications | 68 | 60 | -13% |

## PLANS FOR THE ACRF

We are now in a period of consolidating final plans for the ACRF and developing a program for equipment acquisition. During consultation with the Clinical Center administration, I presented an ACRF equipment budget which outlined the expenditure of approximately $5,400,000 for major equipment purchase and for relocation of recently acquired equipment from the existing to the new Department. In view of continuing rapid developments in the art of computed tomography and the demise of the EMI cooporation, it was decided that plans to equip the CT suites in the new Department would be deferred and that only the perimeter of the ACRF CT suite will be constructed. This decision will permit us maximal flexibility and will also allow us to postpone decisions regarding CT acquisition until such time as more rational decisions can be made. Specifications for major equipment purchases are being developed in the Department and will be submitted to Clinical Center administration later this fiscal year. Final construction plans and individualized diagnostic room specifications are in the hands of the construction engineers and with the exception of the CT suites, all plans for construction have been finalized and work is proceeding on schedule.

### Capital Equipment Acquisition for the Existing Department

During the past year we have ordered and installed a GE 8800 universal CT scanner at a cost of approximately $750,000 and have replaced our 7 year old Special Procedures Room with a Philips Polydirectional Angiographic unit at a cost of $650,000. Additionally ordered and now in storage, is a CGR Polydirectional Film tomographic unit which I plan to install in the existing Department within the next several months to relieve the extremely congested conditions in the Ultrasound Suite. The installation of the CGR tomographic unit will free up space adjacent to the Ultrasound Room and permit expansion of this extraordinarily cramped facility. Acquired at a cost of $285,000, this unit as well as the GE CT scanner and the Philips angiographic equipment will be moved into the ACRF.

### AD HOC Radiology Department Advisory Committee

On December 5 and 6 of 1979, the Department was inspected by a high level committee of academic radiologists, Drs. Abrams, Seimen, Stanley, Taylor and White. The committee studied the operations of the Department with great care and was able to submit what was basically a flattering assessment of Departmental performance. A recapitulation of the summary of the advisory committee is, I think, desirable and follows: "1) Establish Radiology as a research, teaching, and service department - like other clinical services - under the aegis of the National Institutes of General Medical Sciences or a new National Institute of Radiologic Sciences. 2) Support an on-line research budget for Radiology. 3) Develop a center of research imaging as part of the Department, funded by institutes with Clinical Center funds. 4) Double the professional staff size from 13 to 26. 5) Raise staff salary levels so as to be competitive with academic centers. 6) Integrate nuclear radiology into the Department under Dr. Doppman's direction. 7) Initiate comprehensive review by Dr. Doppman and his colleagues of all institute proposals and protocols involving imaging before their implementation." While somewhat grandiose and largely impracti

because of the severe budgetary constraints now placed on all federal departments, the tenor of the report was such as to suggest that further erosion of staff income and fringe benefits coupled with increasing clinical service and teaching responsibilities will discourage retention of staff and severely handicap our recruiting efforts. Suggestions 1, 2, 3, and 6 are, in the present environment, impossible. Success in recruiting and retaining competent staff will require increased attention to providing direct or indirect rewards to the professional staff which are competitive with academic centers.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 04011-03-DR |

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

IV HEPATOSPLENOGRAPHY

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI | Dr. M. Vermess | Associate Chief | DRD CC |
| OTHERS | Dr. R.N. Adamson | Chief | LCHPH NCI |
| | Dr. J.L. Doppman | Chief | DRD CC |
| | Dr. Dulal Chatterji | | PHAR CC |
| | George Grimes | | PHAR CC |
| | Mary Girton | R.T. | DRD CC |

COOPERATING UNITS (if any)

Mallinckrodt Inc., Diagnostic Product Division,
675 Brown Road
St. Louis, MO 63174

LAB/BRANCH
Diagnostic Radiology Department

SECTION

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Results and Current Objectives

The contrast material we have developed in the early years of this project: Ethiodized Oil Emulsion 13 (EOE 13) is now in the stage of clinical trials. We have injected 40 patients to this date for computed tomographic examination of the liver and spleen. A detailed report of our experience with the first 10 patients is in print (Ref. #7). A very significant biodistribution study was performed with EOE 13 labeled with Iodine 125 with the help of the Mallinckrodt Incorporated. The study showed that close to 80% of the injected contrast material is deposited in the liver within 15 minutes following the injection.

With the progression of the Clinical Trials the laboratory work with this contrast material has been reduced. Currently we are examining Rhesus monkeys with induced hepatic cell carcinoma to determine the optimal increase in opacity of the liver to detect small hepatic lesions and improve the diagnosis of hepatic metastases.

## Major Findings

We have shown that this contrast material selectively opacifies the liver and spleen with relatively small doses and significantly improves the diagnostic evaluation of these organs.

## Significance of Research

A new intravenous contrast material was developed (with the utilization of previous French experimental clinical work) which on intravenous injection opacifies the liver and spleen. The contrast material developed in this project is currently undergoing Clinical Phase I Trials.

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6. Vermess M, Inscoe S and Sugarbaker P: Diagnostic pitfalls of the lobulated spleen on computerized tomograms demonstrated with liposoluble intreavenous contrast material. J Comput Assist Tomogr 4:540-543, 1980.

7. Vermess M, Doppman JL, Sugarbaker P, Fisher RI, Chatterji DC, Luetzeler J, Adamson RH, Grimes G and Girton M: Clinical trials with a newly developed intravenous liposoluble contrast material for computed tomographic examination of the liver and spleen. Radiology (In Press)

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 04013-02-DR |

PERIOD COVERED

October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

EVALUATION OF CONTRAST AGENTS FOR TRANSCATHETER ORGAN ABLATION

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI | Dr. J.L. Doppman | Chief | DRD CC |
| | Mary Girton | R.T. | DRD CC |
| OTHERS | Richard Diggs | Technician | DRD CC |
| | Mark Popovsky, M.D. | Pathologist | PATHOL NCI |

COOPERATING UNITS (if any)

LAB/BRANCH

Diagnostic Radiology Department

SECTION

INSTITUTE AND LOCATION

CC, NIH, Bethesda, Maryland 20205

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|---|---|---|
| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Objectives

To evaluate currently used radiopaque agents in a wedge catheter system as a means of achieving parenchymal damage in a variety of endocrine tumors.

Methods Employed

Prolonged staining of parathyroid adenomas following injection of moderate doses of contrast material through a wedge catheter system has led to permanent control of hyperparathyroidism in a small number of clinical subjects. We are investigating in laboratory animals the potential for using this wedge catheter system to permanently ablate organ function without the use of particulate embolizing agents or plastics.

Balloon catheters are used to obstruct arteries into which undiluted contrast material is perfused into the vascular bed of the target organ. Currently, kidneys in a variety of animals are being so treated in an attempt to produce medical

nephrectomy without the risk of embolization. Organs so perfused remain stained for several hours, and absence of urine production in follow-ups ranging 6 to 8 weeks have been demonstrated. Currently under investigation is the need to obstruct arterial inflow following such stainings and the long term results of such interventions.

## Significance of Research

The ability to ablate function of highly specialized tissues, endocrine adenomas, kidneys, without using particulate or non-biodegradable embolizing agents would have significant application. For this reason the use of hypertonic contrast media in a wedge system to produce acute cellular damage is being investigated.

## Publications

Doppman JL, Brown EM, Brennan MF, Spiegel A, Marx SJ and Aurbach GD: Angiographic Ablation of Parathyroid Adenomas. Radiology 130:577-582, 1979.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 04015-02-DR |

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

BIODISTRIBUTION STUDY OF INTRAVENOUSLY INJECTED PARTICULATE SUSPENSIONS

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI | Dr. J.L. Doppman | Chief | DRD CC |
| | Dr. M. Vermess | Associate Chief | DRD CC |
| | Dr. D. Chatterji | | PHARM CC |
| OTHERS | Mary Girton | R.T. | DRD CC |
| | Richard Diggs | Technician | DRD CC |

COOPERATING UNITS (if any)
Outside NIH: B. Halpern, Ph.D., Polysciences, Inc., Warrington, PA
Research Associate

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Diagnostic Radiology Department

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☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Objectives

To determine optimal particle size for a colloidal suspension to be used for increasing absorption coefficients of the liver and facilitate the detection of small hepatic metastases.

Methods Used

There have been considerable unexpected difficulties and delays with the extraction and exact quantitation of the latex particles following intravenous injection. Last year we were finally able to extract these particles with Toluene from the animal tissues and quantitate them by fluorometry. The exact details of the quantitation technique are still under experiment. Once we have finalized the technique, the optimal particle size for hepatic deposition will be determined.

## Significance of Research

We are trying to demonstrate that certain organs preferentially take up intravenously injected particles of specific diameters. This would prove to be a significant help in the development of an ideal intravenous contrast material for the opacification of the liver and spleen and may facilitate earlier detection of small liver metastases on computerized tomographic examinations of the liver and spleen.

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PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

LYMPHOGRAPHY IN ONCOLOGIC PATIENTS

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI | Dr. N. Reed Dunnick | Staff Radiologist | DRD CC |

COOPERATING UNITS (if any)

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Diagnostic Radiology Department

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☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Objectives

To evaluate the role of lymphography in comparison with other diagnostic modalities such as ultrasound and computed tomography in the staging and follow-up of patients with appropriate malignancies.

Methods Employed

Bipedal lymphography is routinely performed on patients with a variety of malignancies, including malignanct lymphomas, testicular tumors, carcinoma of the prostate, carcinoma of the ovary, and mycosis fungoides. Follow-up radiographs are performed at periodic intervals and an evaluation of the opacified retroperitoneal lymph nodes is made to assess disease progression. The results are compared with other modalities to assess their relative value in following patients with underlying malignancy.

## Major Findings

Percutaneous lymph node aspiration has enabled radiologists to clarify equivocal lymphograms and document the presence of tumor. This has been particularly helpful after therapy has altered the appearance of the opacified retroperitoneal lymph nodes.

Lymphography has been useful as one of several modalities in following patients with carcinoma of the prostate. It is limited in part by the relatively poor filling of retroperitoneal lymph nodes in older patients. Bipedal lymphography has thus far been quite useful in patients with testicular carcinoma, ovarian carcinoma, and malignant lymphomas. The better detail provided by lymphography is helpful in small sites of metastatic disease. Extranodal disease is easier detected by computer tomography. Bulky disease can usually be readily identified by either method.

## Literature

1. Dunnick NR, Fisher RI, Chu EW and Young RC: Percutaneous Aspiration of Retroperitoneal Lymph Nodes in Ovarian Cancer. _Am J Roentgenol_ 135:109-113, 1980.

2. Ihde DC, Bunn PA, Cohen MH, Dunnick NR, Eddy J and Minna JD: Effective Treatment of Hormonally-Unresponsive Metastatic Carcinoma of the Prostate with Adriamycin and Cyclophosphamide: Methods of Documenting Tumor Response and Progression. _Cancer_ 45:1300-1310, 1980.

3. Dunnick NR and Harwick A: Lymphography in Patients Following Leg Amputation. _Radiology_ 131:544-545, 1979.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 04017-01-DR |

PERIOD COVERED

October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

ULTRASOUND ANALYSIS OF IRON STORAGE DISEASES

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI | Dr. T.H. Shawker | Chief, Ultrasound Section | DRD CC |
| OTHERS | Dr. M.R. Paling | | DRD CC |
| | Dr. A. Nienhuis | | NHLB CC |
| | Dr. M. Linzer | | NBS |
| | Dr. S. Parks | | NBS |

COOPERATING UNITS (if any)

NHLB; NBS

LAB/BRANCH

Diagnostic Radiology Department

SECTION

Ultrasound

INSTITUTE AND LOCATION

CC, NIH, Bethesda, Maryland 20205

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☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Objectives

Prospective trial of examining ultrasound amplitudes for quantifying amount of iron absorption in the liver and pancreas.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE<br>PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br><br>Z01 CL 04018-01-DR |

PERIOD COVERED

October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

ULTRASOUND ANALYSIS OF OVARIAN STRUCTURES IN PATIENTS UNDERGOING CHEMOTHERAPY

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI | Dr. D.R. Mattison | | NICHD |
| OTHERS | Dr. T.H. Shawker | Chief, Ultrasound Section | DRD CC |
| | Dr. M.R. Paling | | DRD CC |

COOPERATING UNITS (if any)

NICHD

LAB/BRANCH

Diagnostic Radiology Department

SECTION

Ultrasound

INSTITUTE AND LOCATION

CC, NIH, Bethesda, Maryland 20205

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☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Objectives

Ovarian size and structure will be evaluated in those patients suffering ovarian failure following chemotherapy. Patients with both Hodgkin's disease and non-Hodgkin's lymphoma will be examined by both ultrasound and ovarian biopsy.

S-6040

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PERIOD COVERED

October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

ULTRASOUND SCREENING OF ASYMPTOMATIC INDIVIDUALS FOR CHOLOLITHIASIS

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI | Dr. T.H. Shawker | Chief, Ultrasound Section | DRD CC |
| | Dr. A. Dwyer | | DRD CC |
| OTHERS | J. Pearlman | | NCHS |
| | H.P. Roth | | NIAMDD |
| | Knowler | | NIAMDD |

COOPERATING UNITS (if any)

NCHS; NIAMDD

LAB/BRANCH

Diagnostic Radiology Department

SECTION

Ultrasound

INSTITUTE AND LOCATION

CC, NIH, Bethesda, Maryland 20205

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☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Objectives

Mass screening of United States population South West for epidemiology and incidence of asymptomatic gallstones.

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PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

ULTRASOUND ANALYSIS OF DIFFUSE LIVER DISEASE

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI | Dr. T.H. Shawker | Chief, Ultrasound Section | DRD CC |
| OTHERS | Barranger, J.A. | | NIDMN |
| | Linzer, M. | | NBS |

COOPERATING UNITS (if any)

NINCDS; NBS

LAB/BRANCH
Diagnostic Radiology Department

SECTION
Ultrasound

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

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☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Objectives

Analysis of echo amplitude as a technique for following therapeutic response in Gaucher's patients undergoing replacement therapy and for establishing the amount of liver damage due to this disease.

S-6040

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 04021-01-DR |

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

EFFICACY OF ULTRASOUND IMAGING FOR DETECTING LIVER METASTASES

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI | T. Smith | | CC, Surgery |
| OTHERS | T.H. Shawker | Chief, Ultrasound Section | DRD CC |
| | P. Sugarbaker | | CC, Surgery |
| | M. Vermess | Associate Chief | |

COOPERATING UNITS (if any)

CC, Surgery Branch

LAB/BRANCH
Diagnostic Radiology Department

SECTION
Ultrasound

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

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| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |

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☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Objectives

Prospective study comparing ultrasound, CT and nuclear medicine for detecting liver involvement in patients with cancer of the colon.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>NOTICE OF<br>INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br><br>Z01 CL 04022-01-DR |

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

REAL-TIME ULTRASOUND STUDY OF SPEECH

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI | T.H. Shawker | Chief, Ultrasound Section | DRD CC |
| OTHERS | B. Sonnies | | Rehabilitation, CC |
| | T. Hall | | DRS, BEI |
| | B.J. Baum | | NIA |

COOPERATING UNITS (if any)

CC, Physical Therapy Department, Biomedical Engineering
NIA, Laboratory of Molecular Aging

LAB/BRANCH
Diagnostic Radiology Department

SECTION
Ultrasound

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

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☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Objectives

Real-time ultrasonic study of tongue motion in normal and neurologically impaired speech. Longitudinal study will also be performed on aging population to determine if there is any change in motion patterns related to aging.

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 04023-01-DR |

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

ULTRASOUND AMPLITUDE ANALYSIS OF DIFFUSE THYROID DISEASE AND THYROID NODULES

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI | T.H. Shawker | Chief, Ultrasound Section | DRD CC |
| OTHERS | M. Paling | | DRD CC |
| | T. Pretorius | | NIAMDD |
| | M. Linzer | | NBS |
| | S. Parks | | NBS |

COOPERATING UNITS (if any)

NIAMDD, NBS

LAB/BRANCH
Diagnostic Radiology Department

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Ultrasound

INSTITUTE AND LOCATION
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| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |

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☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Objectives

Thyroid B-scan analysis of amplitude of echoes in patients with Graves' disease and Hashimoto's thyroiditis. Clinical techniques will also be developed using both static and real-time ultrasound imaging to increase the yield of thyroid percutaneous aspiration.

PHS-6040
[illegible]

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 04024-01-DR |

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

DEVELOPMENT OF ULTRASOUND REAL_TIME BIOPSY TRANSDUCER

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI | T.H. Shawker | Chief, Ultrasound Section | DRD CC |
| OTHERS | N. Schuette | | DRS, BEI |
| | T. Hall | | DRS, BEI |

COOPERATING UNITS (if any)

DRS, BEI

LAB/BRANCH Diagnostic Radiology Department

SECTION Ultrasound

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☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Objectives

Design and clinical application of ultrasound transducer incorporating real-time imaging and biopsy capability.

| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 04025-01-DR |
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PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

DETECTION OF PULMONARY METASTASES BY COMPUTED TOMOGRAPHY

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI N. Reed Dunnick, M.D. DRD CC

COOPERATING UNITS (if any)

LAB/BRANCH
Diagnostic Radiology Department

SECTION

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☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Objectives

The detection of pulmonary metastases at the earliest possible time and the differentiation of benign pulmonary nodules from metastases.

Methods

Patients who are surgical candidates are examined by CT. Suspicious areas of the lung are measured to determine the relative density as well as size and configuration characteristics. These results are then correlated with the pathologic interpretation.

PHS-6040
(Rev. 10-76)

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| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 04026-01-DR |

PERIOD COVERED

October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

LOCALIZATION OF FUNCTIONAL ADRENAL TUMORS

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | |
|---|---|---|
| PI | N. Reed Dunnick, M.D. | DRD CC |

COOPERATING UNITS (if any)

LAB/BRANCH

Diagnostic Radiology Department

SECTION

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☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Objectives

Patients with functional tumors of the adrenal gland can be identified and confirmed by laboratory measurement of the appropriate hormone. We hope to localize the tumor to allow a less morbid surgical procedure.

Methods

Patients with functional adrenal tumors are examined by CT, ultrasound, selective adrenal vein sampling, and in many cases arteriography. The results are then compared with surgical and pathologic findings.

[illegible]-6040
[illegible]

October 1, 1979 through September 30, 1980

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES

CLINICAL CENTER

ENVIRONMENTAL SANITATION CONTROL DEPARTMENT

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October 1, 1979 through September 30, 1980

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES

CLINICAL CENTER

ENVIRONMENTAL SANITATION CONTROL DEPARTMENT

## MISSIONS AND GOALS

The primary objectives of the Environmental Sanitation Control Department during the year were to:

1. Provide a dependable, efficient, elevator service responsive to the requirements of patients, emergencies, staff, and visitors.
2. Provide the safest possible sanitary environment for the Institutes and services in the Clinical Center.
3. Study the Department's manpower requirements and formalize its work and personnel procedures.
4. Orient, train, and supervise its personnel so that they are proficient in carrying out the program objectives.
5. Test various products and equipment in order to utilize the most modern housekeeping practices.
6. Cope with day-to-day environmental problems within the Clinical Center and study the total environmental problems within the Clinical Center as they relate to an institutional setting.
7. Develop an objective evaluation of the housekeeping program.
8. Establish a new section for A.C.R.F.

## DEPARTMENT SENIOR STAFF

The Department Senior Staff (7) has a combined total of one hundred and seventy nine years of government service; one hundred and twenty years of

service time was spent in the Environmental Sanitation Control Department.

## DEPARTMENT ACTIVITIES

There have been three promotions to supervisor; 11 promotions to leader; 1 promotion to Assistant Chief, NSS.

Employee turnover was higher than the previous year with sixty-six new employees entering on duty and sixty-eight leaving. Table 2 shows that 24 resigned, 5 transferred, 4 retired, 35 were terminated.

Individual employees and groups received 25 letters of appreciation or commendation from building tenants for services rendered. Superior performance awards were awarded to eight supervisors and thirty-two housekeeping aids and leaders.

The Department coordinated the selection, procurement, and installation of approximately 1,250 yards of carpeting during the year. This includes replacing 400 yards of existing carpeting. We have been able to find 4 carpet qualities within GSA Contract Schedules that meet DHHS standards.

Locker room renovations - B1B-19A locker room is nearly complete, enabling ESCD to relocate Clinical Center staff from B1D-25 to B1B-19A so renovations could start in B1D-25. The move was completed with few problems.

Elevators in ACRF have been included in the contract with Clinical Center elevator maintenance. Service has improved and these elevators are now automated.

We are testing the compactors on each floor and plan to phase out GI cans in the Clinical Center before September 1, 1980. We have also implemented and tested a back-up system for waste removal in case both compactors are down at the same time.

## MAJOR PROGRESS IN RESEARCH, SERVICES, TRAINING AND DEVELOPMENT

Construction of the ACRF and building renovations continued to present the Department with its greatest challenge. In addition to uncounted minor projects during the year, there were several major projects affecting all areas of the building. While renovations are in progress, the natrual reaction is to throw in the dust towel and give up on housekeeping until conditions settle and housekeeping can be handled in a normal routine fashion. However, renovations create conditons which call for an actual intensification of housekeeping activities. There is a very real problem of maintenance becoming considerably more difficult, both from a psychological and practical performance standpoint, while at the same time efficiency becomes more important.

The Department experiences major inconvenience because of flooding in the Clinical Center and ACRF garage. This made necessary the purchase of 7 additional 55-gallon wet-pickups.

Construction of the ACRF created many novel problems for the ESCD: areas adjacent to the construction had to be protected from contamination by the soils and waste material produced in renovation; floors became badly damaged by scratching or abrading from tracking in the particles of concrete, metal chips, splinters, mud, etc; airbourne waste particles and dust could damage office equipment and mechanical systems. Comfort became an important factor since people react to unpleasant conditions caused by excessive dust and soil. Infection control became more difficult. The basic housekeeping principle during ACRF construction renovation has been isolation: the remodeling work and its byproducts have been completely isolated from the portion of the building not involved. Some of the more effective steps in

this direction are containment barriers around the work area, mats and runners in connecting areas to entrap as much soil and dirt as possible, and restriction of sightseer's walking through the area and tracking soil back into other areas.

Special Elevator Service - ESCD responded to 15,407 special elevator service requests (279 man hours) and 100 additional O.R. requests (33 man hours). Elevators were out of service 344 times (2,610 hours).

ESCD assisted Plant and Engineering Section with Clinical Center Emergency Generator test.

The emergency assistance program for the Department operated satisfactorily during the year. Elevator operators and others were briefed several times on emergency procedures. Water pick-up equipment was renovated and replaced during the year and operated in a very satisfactory manner. The following emergencies were encountered during the year:

| | | |
|---|---|---|
| Floods: | 100 calls for | 546 staff hours |
| Fires: | 5 calls for | 229 staff-hours |
| Electrical: | 20 calls for | 6 staff-hours |
| Others: | 36 calls for | 11 staff-hours |

Ten cleaning products were evaluated: three stainless steel cleaners; 1 graffiti remover; two dust treatments for dry mops; 1 germicidal cleaner; three floor sealers. Of these products, six were unsuitable for use in the Clinical Center. One sealer, two dust mop treatments and the graffiti remover were selected for more testing.

We purchased (9) foldaway double tank maid's carts; (7) multispeed buffers; (8) microstat vacuums; (2) battery powered floor polishers; (1) 560B Retreiver battery powered heavy sweeper for ACRF garage and (1) electric mop treater.

## FUTURE OBJECTIVES DIRECTED:

1. Implement new solid waste handling system based on reactivation of existing Clinical Center trash chutes.

2. Complete refresher training and certification in basic work procedures for all Department supervisors, leaders, and employees.

3. Support and encourage upward mobility for employees so that they may work at their fullest potential.

4. Continue to study the feasibility of phasing out manual passenger elevator service and converting to automatic passenger elevators.

5. Publish new cleaning procedures in "Clinical Center Cleaning Procedure Manual," and revise 25% of programmed work plans.

6. Continue to test new products and equipment.

7. Coordinate selection of textiles and fabrics for draperies, furniture, and wall and floor coverings within the Clinical Center.

8. Establish training program for ACRF garage maintenance crew.

9. Establish review training for all employees twice yearly for "Waste Handling" emphasizing correct procedures for Infectious and Radioactive waste.

## TABLE 1

## ENVIRONMENTAL SANITATION CONTROL DEPARTMENT

OCTOBER 1, 1979 through September 30, 1980

| GOVERNMENT | | STAFF HOURS | |
|---|---|---|---|
| Civil Service | | | |
| EEO Training | | 80 | |
| Employee Assistant Program | | 280 | |
| Educational Program | | 300 | |
| Adult Education | | 768 | |
| Fire Safety Training | | 64 | |
| 2-Day Seminar on Retirement Planning | | 40 | |
| Supervisor Seminars | | 400 | |
| NON-GOVERNMENT | | | |
| Upward Mobility College | | 30 | |
| | TOTAL | | 2076 |
| WITHIN DEPARTMENT | | | |
| Procedures and Orientation | | 3640 | |
| All Employee Training | | 2760 | |
| | TOTAL | | 6400 |
| | GRAND TOTAL | | 8476 |

## TABLE 2

## POSITIONS FILLED BY RECRUITMENT

## ENVIRONMENTAL SANITATION CONTROL DEPARTMENT

## OCTOBER 1, 1979 THROUGH SEPTEMBER 30, 1980

| MONTH | GENERAL SCHEDULE | OTHER WAGE BOARD | WG-03 | WG-02 | WG-01 | TOTAL |
|---|---|---|---|---|---|---|
| OCTOBER | | | | 2 | 1 | 3 |
| NOVEMBER | | | | 19 | 3 | 22 |
| DECEMBER | | | | 3 | 1 | 4 |
| JANUARY | | | | | 1 | 1 |
| FEBRUARY | | | | 4 | 4 | 8 |
| MARCH | | | | 14 | 1 | 15 |
| APRIL | | | | 6 | 1 | 7 |
| MAY | | | | | | |
| JUNE | | | | | | |
| JULY | | | | 6 | | 6 |
| AUGUST | | | | | | |
| SEPTEMBER | | | | | | |
| SUB-TOTAL | | | | 54 | 12 | 66 |

* Total includes 50 1-year temporary appointments and 16 career condition appointments.

## TABLE 3

## NUMBER OF SEPARATIONS; RESIGNATIONS, BY MONTH AND GRADE

## ENVIRONMENTAL SANITATION CONTROL DEPARTMENT

## OCTOBER 1, 1979 THROUGH SEPTEMBER 30, 1980

| MONTH | GENERAL SCHEDULE | OTHER WAGE BOARD | WG-03 | WG-02 | WG-01 | TOTAL |
|---|---|---|---|---|---|---|
| OCTOBER | | | 1 | 17 | | 18 |
| NOVEMBER | | | | 3 | 1 | 4 |
| DECEMBER | | 1 | | 3 | 1 | 5 |
| JANUARY | | | 1 | 3 | 3 | 7 |
| FEBRUARY | | | 3 | | | 3 |
| MARCH | | 1 | 1 | 4 | | 6 |
| APRIL | | | 1 | | | 1 |
| MAY | | 1 | | 5 | | 6 |
| JUNE | | | | 6 | | 6 |
| JULY | | | | | | |
| AUGUST | | | | 1 | | 1 |
| SEPTEMBER | | | | 9 | 2 | 11 |
| SUB-TOTAL | | 3 | 7 | 51 | 7 | 68 |

## TABLE 4

## REASONS FOR PERSONNEL LEAVING

## ENVIRONMENTAL SANITATION CONTROL DEPARTMENT

## OCTOBER 1, 1979 THROUGH SEPTEMBER 30, 1980

| RESIGNATIONS | TRANSFERS | RETIREMENTS | TERMINATIONS | DECEASED |
|---|---|---|---|---|
| Resigned when faced with possible disciplinary action 7 | Improve career opportunities 4 | Retirement disability 1 | Separation during probationary period 2 | |
| To accept non-government positions 9 | Transportation | Retirement optional 3 | Termination of temporary appointment 1 | |
| Moving Away 2 | Higher Salary 1 | | Expiration of temporary appointment 30 | |
| Health 4 | | | Abandonment of position 2 | |
| Personal 2 | | | Failure to report for duty | |
| SUB-TOTALS 24 | 5 | 4 | 35 | |

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# FABRIC CARE DEPARTMENT

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## FABRIC CARE DEPARTMENT

## I. MISSION AND GOALS

The primary objectives of the Fabric Care Department during Fiscal Year 1980 were to:

1. Provide quality fabric care services at the most reasonable cost consistent with the needs of patient care and research in the Clinical Center and other N.I.H. installations on the Bethesda campus, the Poolsville animal farm, the Landau, Westwood, Auburn buildings, the Baltimore Cancer Research Center, and St. Elizabeth's Hospital;

2. Renovate the dry cleaning plant in accordance with Environmental Health and Safety Standards;

3. Procure and install new garment team folder;

4. Continue to review manpower requirements in an effort to keep the number of permanent, full-time positions to at least three positions below the authorized N.I.H. ceiling;

5. Provide in-service training for all employees;

6. Continue to improve the quality of service to the N.I.H. community at a reasonable cost;

7. Complete evaluation and install electronic dispensing system on all wash machines.

## II. ACTIVITIES

### A. Production

Laundry Operations:

| | |
|---|---|
| Pounds Washed and Finished | 1,940,778 |
| Pounds Dyed | 45,465 |

Dry Cleaning Operation:

| | |
|---|---|
| Pounds Dry Cleaned and Finished | 74,237 |

New Linen Stores:

| | |
|---|---|
| Items Issued | 33,651 |
| Items Repaired | 2,280 |
| Items Altered | 24,693 |
| New Items Fabricated | 501 |
| Opening Inventory | 594,679 |
| Purchases | 473,526 |
| Cost of Goods Sold | 444,083 |
| Stock Write-Off | 110 |
| Closing Inventory | 701,250 |

1. The Department was able to meet the normal demands for service with no major problems and with three positions below the authorized ceiling.

2. A new oil burner and boiler were installed.

3. Budgeted overtime was reduced by 10%.

4. JCAH conducted a survey of the Department.

5. Twelve new linen carts were procured to provide more efficient service.

### B. Personnel

1. The Department provided training and work experience for two Stay-in-School employees.

2. Two employees attended a EEO workshop sponsored by NIH. (48 man hours).

3. Plant Superintendent completed a course at the American Laundry and Linen College sponsored by NAILM. (40 man hours).

4. Two employees attended and completed a course at IFI, International Fabricare Institute, on dry cleaning and wash procedures - (80 man hours).

5. One employee attended and completed a two week course at International Fabricare Institute on laundry management, washroom procedures, and linen control - (80 man hours).

6. The chief of the Department attended the 40th Annual Educational Conference of N.A.I.L.M.

## III. FUTURE OBJECTIVES

1. Renovate the dry cleaning plant in accordance with Environmental Health and Safety Standards.

2. Continue to review manpower requirements in an effort to reduce authorized permanent full-time ceiling by one position.

3. Install new garment team folder.

4. Continue to participate in the Stay-in-School and the Summer-Aid programs.

5. Reduce budgeted overtime by 10%.

6. Reduce 1981 budget by 5%.

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MATERIEL HANDLING DEPARTMENT

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# MATERIEL HANDLING DEPARTMENT

## I. MISSION AND GOAL

The Materiel Handling Department was officially organized on October 1, 1979, with the consolidation of Central Sterile Supply Service (from the Pharmacy Department), Transportation and Property Management Section, and Central Services Section (from the Office of Administrative Management). The Materiel Handling Department was conceived from the need for the integration and management of materiel support functions. The impetus was the advent of the ACRF and new automated distribution systems, which made such integration feasible.

The mission of the Department is to integrate the functions of purchasing, administrative services, forms management, supply, distribution, processing, property management, equipment management, space management, and receiving and shipping into a cohesive materiel management operation. The goal is to provide a service responsive to the materiel support requirements of patient care as well as to the distribution of materiel for the occupants of the Clinical Center.

The Department's five major goals prior to full occupancy of the ACRF are these:

1. Integration of distribution systems;

2. Minimization of staff involved in materiel distribution;

3. Improvement of space utilization required for materiel management functions;

4. Maintenance of an equipment management program; and

5. Providing an interface for the Clinical Center with the NIH-wide Materiel Management System.

The Materiel Handling Department consists of Central Sterile Supply Section, Hospital Administrative Services Section, Receiving and Distribution Section, and the Office of the Chief.

Central Sterile Supply Section provides 24 hour service in supplying medical equipment and medical-surgical supplies for patient care as well as ancillary supply services, such as patient television sets and isolation protocol linen. The Section decontaminates, processes, assembles, sterilizes, and issues a variety of packs, trays, sets, instruments, and utensils. It also procures supplies from NIH supply sources, as well as from private vendors and contractors. This involves the maintenance of a procurement and supply operation administering a delegated procurement authority as well as an inventory control and supply function. Supplies are issued via an exchange cart systems, PAR-stocking and direct requisition issue.

The Hospital Administrative Services Section is responsible for hospital wide documentation procedures i.e., policies and procedures for forms development an control, files analysis and design, and records scheduling and disposition. The Section is also responsible for service functions such as graphics, office equipment acquisition, and copying service for the Clinical Center organization.

The Receiving and Distribution Section provides distribution of materiel received at the B-1 level loading dock and via the tunnel from Building 13, to occupants of the Clinical Center. This includes distribution of materiel ranging from ice, to animal food and bedding. The Section also provides relocation and moving services for furniture and equipment. Property management serivces are also provided. Custodial areas are assisted in updating property lists, recording capital property, disposing of surplus property, as well as providing a search service for Clinical Center property needs.

The Office of the Chief integrates the materiel functions of the three Sections and provides policy direction and development in meeting the Department's mission and goals. It also functions as the Clinical Center liaison with the branches of DAS involved in materiel management. The Office of the Chief provides the Clinical Center Executive Office with policy recommendations concerning the integration of materiel services, especially as they relate to Clinical Center construction programs.

## II. DEPARTMENT ACTIVITIES

The first month of the Department's existence was spent in establishing self-support systems for the new organization. This required extension of operations in Central Sterile Supply to 24 hours, recruitment and training of secretarial staff acquisition of procurement authority from DAS for the Materiel Handling Department, assumption of responsibility for direct issue of Central Sterile Supply take-home supplies to patients, and timekeeping and payroll functions. The identity of the new organization had to be established among the employees, and Department wide policies and procedures were developed.

Certain nursing equipment storage and issue functions were transferred to the Central Sterile Supply Section. Equipment was inventoried, repaired and space was consolidated. The equipment was made available through the computerized Medical Information System requisition process.

The responsibility for the issue and care of the hypo-hyperthermia machines was transferred from the Surgical Services Department to Central Sterile Supply. Centralization of responsibility for the supply of the cardiac emergency carts was achieved by the Materiel Handling Department absorbing the work and supplies formerly provided for the carts by the Anesthesia Support Section, Surgical Services, and the Respiratory Therapy Section, CCM.

The function of issuing emergency isolation linen to the nursing units was transferred to Central Sterile Supply by the Fabric Care Department.

The responsibility for procurement and issue of vacuum system regulator gauges was transferred from the Respiratory Therapy Section, CCM, to Central Sterile Supply Section. Dialysis equipment and supplies were incorporated into the CSS supply system relieving Dr. Balow's staff of this responsibility and providing space to the Respiratory Therapy Section, CCM.

The Hospital Administrative Services Section has taken over Contract Administration and issue responsibilities for patient television sets from the Outpatient Department and the Executive Office.

The delivery of intravenous sets and solutions to Pharmacy was begun by the Central Sterile Supply and Receiving and Distribution Sections. Formerly, the Pharmacy Department was responsible for loading and transporting their own supplies.

A PAR-stocking system was introduced on Nursing Unit 10D, which frees the 10D staff from most requisitioning tasks.

## III. MAJOR PROGRESS IN SERVICES, TRAINING AND DEVELOPMENT

On August 11, 1980 the Materiel Handling Department assumed responsibility for the distribution of all of the Pharmacy Department's unit dose drug carts. This function is performed after 12 midnight, seven days a week. A position from the Pharmacy Department was transferred to the Materiel Handling Department for this purpose.

The Office of the Chief has been involved in the procurement of all equipment for the ACRF. This has included determining needs with the program managers (Surgical Service, Clinical Pathology, etc.), developing selection strategies and integrating the impact of the procurements on architectural/engineering aspects with the Engineering Design Branch and Turner Construction Company. Strategies were provided to the Executive Office as to which procurements should be submitted in FY 80 and which could be deferred. The requisition/justification process for 2.261 million dollars was handled. The TSO Requisition Tracking System was used to provide procurement and financial status of the procurement actions. A process was begun of identifying and coordinating delivery schedules which best accommodated contruction scheduling, availability, and occupancy dates.

The MMS (Materiel Management System) was initiated for direct input of procurement actions and receiving information by the Materiel Handling Department. This will ultimately allow the Department to process all receiving into Building 10 as well as expand procurement services to Clinical Center Departments. The auditing and forwarding of purchase orders was transferred from the Budget Office, Clinical Center, to the Office of the Chief, Materiel Handling Department. This provided a means for scheduling deliveries and for performing audits on procurement activities within the Clinical Center.

Major modifications to the automated delivery system were recommended by the Office of the Chief. All but one were accepted, redesigned and incorporated into the ACRF construction. The remaining recommendation, involving a direct extension of the automated delivery system to the Building 13 laundry was deferred as a result of unavailable funding. The modifications will result in significant improvement in utility of the automated delivery system.

Responsibility for the coordination of occupancy moves into newly constructed facilities has been given to the Office of the Chief. This involves scheduling a variety of pre-occupancy milestones and coordinating the elimination of obstacles that effect the critical path for meeting the scheduled occupancy. Part of this responsibility has required early involvement in the modernization process at the point of facilities design and procurement planning.

The Medical Device Evaluation and Standardization Committee was established as a subcommittee of the Clinical Center Safety Committee as a direct effort of the Materiel Handling Department's goal to develop an equipment management program. The committee has served as a highly responsive vehicle to make recommendations concerning medical device procurements and obtaining state-of-the-art equipment for medical care.

The new ACRF Central Sterile Supply facility was reprogrammed and redesigned to reflect a number of technological advances, JCAH requirements and projected expanded services. Final redesign was completed in August 1980.

A number of training courses were attended which related to the management tools needed to develop the Materiel Handling Department: Small Purchasing, Basic Procurement, Basic Project Management, FES Classification System, The Federal Budget Process and Personnel Adverse Actions.

Monthly in-service training is provided in Central Sterile Supply Section for the Medical Aids. This serves as documented in-service training necessary to meet JCAH requirements.

A course in ethylene oxide use in sterilization is being prepared by the Materiel Handling Department through the auspices of the Safety Committee, Clinical Center, for certification in the use of ethylene oxide.

## IV. FUTURE OBJECTIVES

Fiscal Year 1981 will require the full development of the Materiel Handling Department's organization into a complete materiel management function in order to coincide with the completion and occupancy of the ACRF and operational functioning of the automated delivery systems. Initial occupancy is expected in April 1980.

The Materiel Handling Department will be reorganized into four new Sections, establishing a separate Distribution Section, Receiving and Property Management Section, a Central Hospital Supply Section, and inclusion of procurement activities into the Hospital Administrative Services Section.

The Distribution Section will emphasize the important goal of providing a responsive distribution operation of all materiel to all occupants of Building 10. This will include management of the extensive automated delivery systems and the establishment of "floor managers" serving as regional materiel managers interfacing with the Institute administrative functions and with the Clinical Center program coordinators. The Section will emphasize the use of Program Evaluation and Review Techniques (PERT) for regimentalized scheduling, as well as utilization of evening and night shift delivery capability of the automated systems.

The Receiving and Property Management Section will emphasize capturing receiving data into the MMS and the inspection and property accountability management with the impetus on monitoring the medical device recall system that will be established.

The Central Hospital Supply Section will be responsible for specializing in the centralized sterilization and decontamination of all instrumentation and medical/surgical supplies for the Clinical Center. Emphasis will be placed on the development of a surgical case cart system for the surgical suites and cath-

eterization laboratories. This Section will also provide inventory management and centralization of supply requirements for the Clinical Center organization. Emphasis will be placed on determining the best method of supply and on the dependence of inventory management evaluation techniques (i.e., EOQ, ROP values).

The Hospital Administrative Service Section will expand its role by absorbing all procurement functions within the Clinical Center organization. Emphasis will be placed on the development of a catalog/source advice service and facilitation of procurement actions of the Clinical Center organizations through the NIH procurement process.

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## MEDICAL RECORD DEPARTMENT

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## MEDICAL RECORD DEPARTMENT

## DEPARTMENT MISSIONS AND GOALS

The Clinical Center Medical Record Department maintains a medical record and/or microfiche for every registered Clinical Center patient. The prime objective of the Medical Record Department is to insure that each medical record is complete, accurate, safeguarded, and available to authorized personnel. To this end systems are maintained which provide: 1) immediate access and release of medical records and/or microfiche and information to authorized users; 2) a computerized listing of diagnosis and operation for discharged inpatients; 3) an analysis by Institute of discharged inpatients; 4) a systematic arrangement of reports within the medical record; 5) transcribed medical reports and communication with referring physicians.

## ACTIVITIES AND PROGRESS

### Education and Training

Medical Record Administrators attended the American Medical Record Association's annual convention in Washington, DC, October 24-25, 1979.

Clinical observation affiliation was provided (February 11-22, 1980) for two students from the Department of Medical Record Administration, College of St. Scholastica, Duluth, Minneosta,

The Chief, Medical Record Department and two medical record administrators participated on the Medical Record Improvement Committee, an Ad Hoc committee chaired by Dr. Griff T. Ross, Deputy Director, Clinical Center. The committee's charge was to decrease the bulk and increase utility of the Clinical Center medical records.

Personnel attended a variety of workshops to enhance knowledge of such subjects as microfilming techniques, Privacy Act applications and small purchase procedures.

### Activities and Progress

The Joint Commission on Accreditation of Hospitals conducted its accreditation survey of the Clinical Center on October 16-18, 1979. The survey team evaluated the Medical Record Department services and recommended that:

- --space for the Medical Record Department be increased to accommodate the current workload. It was recognized, however, that the ACRF and Building 10 renovation would alleviate the problem.
- --other suggestions highlighted the need for improving documentation; e.g., various medical and service departments.

## Transcription Services

Contract Modification: Plans for direct dial dictation of medical reports and Outpatient Department letters to a predetermined contractor site were completed. Included in the final phase were:

- --visits to contractor sites by Department Chief and Project Officer to assure smooth transition;
- --satisfactory relocation of Medical Record Department recording equipment to contractor site;
- --investigation and purchase of teletype equipment to provide instantaneous transmission of reports; e.g., stat transcription, source documents.

Reduction in Transcription Contractors: On December 31, 1979, subsequent to contract modification, one contractor elected not to renew the transcription contract. A second contractor defaulted on May 27, 1980, leaving one contractor to perform all transcription services for medical reports. This has resulted in a savings to the Clinical Center due to the efficiency of the sole contractor.

## Microfilm Services

Off-Site Location: Approximately 65,000 active and inactive medical records located in Building 10, Room B2L406, were relocated to an office site at 656 Quince Orchard Boulevard, Gaithersburg, Maryland. Personnel responsible for maintaining the records and preparing the records for the microfilming shuttle between the Clinical Center and the satellite location on a daily basis.

Modification to include reproduction services: Modifications to the existing microfilm contract were made to accommodate the photocopying needs of the Medicolegal Section.

## Coding Classification

The Chief of the Medical Record Department is placing major emphasis on updating the coding classification system for the retrieval of inpatient diagnoses and operations. This included:

- --insuring compatibility between ICDA 8 and ICD 9 by cross-referencing data files;
- --providing specified NIH codes required for data retrieval.

Requests for 1979 studies became available as the reclassification process progressed.

## Automated (Word Processing) Equipment

Two key pieces of equipment were leased to accommodate the tracking of incomplete records and complete records circulated. The equipment enabled the Department to provide monthly institute delinquency listings and monthly follow-up letters relating to records not returned from circulation.

## WORK PRODUCTION STATISTICS

July 1, 1979 to June 30, 1980 -- Actual
July 1, 1980 to September 30, 1980 -- Projected

| | Column A<br>7/1/79-6/30/80<br>(Actual) | *Column B<br>7/1/80-9/30/80<br>(Projected) | Column C<br>TOTAL |
|---|---|---|---|
| I. Medicolegal Section | | | |
| Total number of requests | 13,729 | 2,725 | 16,454 |
| Average requests per day | 42 | 44 | 43 |
| II. Record Processing Section | | | |
| Incomplete records as of 6-30-80 | 1,047 | -- | -- |
| Incomplete records as of 9-30-80 | -- | 1,179 | 1,113 |
| III. Files Section--Record Circulation | | | |
| Complete Records | 20,867 | 5,479 | 26,346 |
| Clinics & Admissions | 59,541 | 14,087 | 73,628 |
| Incomplete Records | 12,778 | 33,149 | 15,927 |
| IV. Transcribing Section | | | |
| Total number of reports transcribed | 16,304 | 4,628 | 20,932 |

* Projected figures 7/1/80-9/30/80 are based on actual figures 7/1/79-9/30/79.

## PROBLEMS

A critical shortage of filing space for active medical records has required relocation of current multipart active medical records to the Gaithersburg satellite location.

Failure to have the medical record responsibilities of paramedical personnel clearly defined has impeded the timely completion of medical reports.

## OBJECTIVES

Computerized System: Finalize decisions concerning available alternatives:
- --track incomplete and delinquent medical records with the capability of a notification system to physicians;
- --track medical records in circulation;
- --automatic equipment and system for filing and retrieving medical records.

Microfilm System: Develop a plan for an ongoing microfilm program for filming active medical records.

Publication of the Medical Record Handbook which contains minimum medical record requirements and confidentiality regulations.

Implementation of an audit system of minimum medical record requirements.

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DEPARTMENT OF NUCLEAR MEDICINE

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# DEPARTMENT OF NUCLEAR MEDICINE

The Department of Nuclear Medicine is divided into four sections; Diagnostic Imaging, Applied Physics, Whole Body Counter, and Radiopharmacy. The primary mission of the Department is to provide nuclear medicine support to the research efforts of the various Institutes by extending diagnostic service to patients who are being studied by NIH physicians.

## DEPARTMENT MISSIONS AND GOALS

### Applied Physics Section

The Applied Physics Section performs two basic functions: 1) to supply technical and professional assistance to the Department of Nuclear Medicine and other investigators in the resolution of selected diagnostic and experimental problems requiring Nuclear Medicine technology and 2) to independently develop novel diagnostic procedures, from concept through hardware, aimed at resolving selected problems of medical diagnosis.

### Diagnostic Imaging Section

This Section serves the clinical research goals of the NIH through the *in vivo* diagnostic use of radioactive pharmaceuticals to evaluate diseases that are under study in the Clinical Center in- and outpatients. This information helps physicians to choose and assess therapy. Major goals are to improve existing techniques and to develop new techniques that have minimal morbidity for the patient. Consultation is provided by the Department's physicians who interview and administer radiopharmaceuticals to all referred patients. Further consultation is rendered by nuclear medicine physicians' attendance at Institute clinical conferences where patient clinical data is reviewed with nuclear medicine input.

### Radiopharmaceutical Section

The major responsibilities of the Radiopharmaceutical Section are its service functions and research efforts. This involves the procurement, receipt, formulation, quality control, research and development, dispensing and record keeping of all radioactive materials intended

for patient administration in Clinical Center patients. A variety of tests necessary to establish the pharmaceutical quality of the products are performed, including the determination of assays, radiochemical and radionuclidic purity checks, pH levels, particle sizing, and biological testing.

### Whole Body Counter Section

The NIH Whole Body Counter Section provides the NIH community with a unique facility for direct quantitative measurements of uptake and retention of biologically active materials and trace elements labeled with gamma-ray emitting radionuclides and evaluation of the amount and identity of unknown radionuclides in the human body. It also serves as a source of information and support for investigators desiring to design special counting systems to measure biological samples containing radionuclides.

## DEPARTMENT ACTIVITIES

### Applied Physics Section

In accord with its mission, the Applied Physics Section continued its collaborative efforts with National Heart, Lung, and Blood Institute/ Cardiology Branch, Division of Computer Research and Technology/ Laboratory of Applied Studies, and DCRT/Computer Systems Laboratory during FY 80 in the pursuit of noninvasive methods for detecting, diagnosing, and quantifying cardiac disease.

Imaging equipment, work space, and expendables were provided by Nuclear Medicine/Clinical Center and DCRT. Radiopharmaceuticals were provided by the Radiopharmacy Section/NM.

### Diagnostic Imaging Section

The imaging equipment necessary to achieve the above mission requires continued upgrading. The required upgrading was achieved in FY 80. The field of nuclear medicine is fast changing and demands a constant refreshment of departmental physician and technician knowledge. Attendance of at least 50% of departmental staff at the regional and national meetings of the Society of Nuclear Medicine was achieved in FY 80. Department members conducted teaching sessions at the national meeting of the Society of Nuclear Medicine in FY 80 and taught at National Naval Medical Center, University of Maryland, Johns Hopkins, and other institutions.

The Department purchased a new large-field-of-view (LFOV) gamma camera (Raytheon Corp.) in FY 80. NINCDS purchased and installed a positron tomographic scanner (ORTEC) in FY 80. To support the Positron Program at NIH, two radiochemists have worked closely with Naval Research Laboratory (NRL) utilizing the NRL cyclotron for the production of positron-emitting radiopharmaceuticals. Patient studies have begun in cooperation with NINCDS and NIMH by scanning patients with Fluorine-18, 2-Fluorodeoxyglucose.

## Radiopharmaceutical Section

Approximately 85% of the total requests and workload of this Section is directed to providing service for the Diagnostic Imaging Section. The future workload can be anticipated to be proportional to that of the Diagnostic Imaging Section in regard to its usage of radionuclide products.

A radiopharmacist continued to be involved in the dosing area and effectively controlled and dispensed radiopharmaceuticals and insured the practice of good radiation safety principles. The Section also implemented endotoxin sensitivity testing employing Limulus Amebocyte for products having radionuclides with a short physical half-life which were destined for parenteral administration.

Two papers were presented at the annual meeting of the American Pharmaceutical Association within the session on radiopharmacy. One of the papers presented a comparison of three commonly employed instruments utilized in determining radiochemical purity and the other summarized a study which determined the various parameters that effect the delivered dose of a radiopharmaceutical product.

## Whole Body Counter Section

The Section has been involved in cooperative studies with researchers at Georgetown University Medical School and the V.A. Hospital and University of Maryland Hospital, Baltimore, in studies of zinc metabolism in subjects with and without diseases. A new research study of the efficacy of total parenteral nutrition for cancer cachexia will be initiated in FY 81 and will involve multiple tracer techniques applied to the evaluation of indices of body composition and nutrition. These studies will be carried out in cooperation with the Division of Surgery, NCI.

The Whole Body Counter Section has emphasized medical research measurements for the past seven years, and will continue to do so during FY 80. Efforts to inform the NIH community of the availability of our services will continue to include the distribution of an informative pamphlet (Whole Body Counter Handbook, DHEW Pub. No. (NIH) 78-348) and the presentation of information about whole body counting and teaching programs for licensed investigators who use radionuclides, available through the Radiation Safety Branch, Division of Safety.

Appended tables provide a complete breakdown of the number and types of studies performed by the Section in FY 80. The Whole Body staff was involved in publication of five papers (3 published, 2 in press), and presentation of two papers (one at the Annual meeting of the Federation of American Societies for Experimental Biology in Anaheim, California and one to the annual meeting of The American Clinical Research Society in Washington, D.C.

## MAJOR PROGRESS IN RESEARCH, TRAINING AND DEVELOPMENT

### Applied Physics Section

Four objectives were attained by the APS during FY 80 in support of collaborative projects with other NIH organizations: (1) APS technical and scientific support continued, as planned, throughout FY 80 as part of a large scale clinical evaluation of gated blood pool imaging at rest and during exercise in patients with a variety of cardiac disorders (CB/NHLBI, APS); (2) a computer-based imaging system was acquired by the APS for CB/NHLBI, for use in the CB animal laboratory. Collaborative studies (CB/APS) using this system with APS developed and supplied software were initiated; (3) continued development and evaluation of a portable probe device capable of direct, continuous monitoring of left ventricular function simultaneously with other physiologic parameters (CSL/DCRT, APS); (4) continued projects and initiated others designed to determine the absolute accuracy of gated blood pool imaging and to absolutely quantitate left ventricular volume.

### Diagnostic Imaging Section

Patient studies utilizing positron transaxial scanning commenced in FY 80.

A physician trained in radiology entered the Department's training program in nuclear medicine. In addition, a physician from the People's Republic of China, Peking Cancer Institute, joined the Department for additional training in nuclear medicine. X-ray CAT studies were terminated with removal of the X-ray CAT machine.

Further developments in gated pulmonary studies have been achieved in cooperation with the Pulmonary Branch/NHLBI. New clinical research applications and improved computer methods were employed in FY 80. Ongoing support of clinical research projects was provided, involving the clinical branches of these institutes. NCI, NIAMDD, NHLBI, NICHD and NIAID.

### Radiopharmaceutical Section

A total of 25 different radionuclides comprising 63 different products were received, registered, and formulated. Research and development was focused on the radiopharmaceutical aspects of positron emitting radionuclides, namely Fluorine-18 and Gallium-68. Fluorine-18 as 2-Fluorodeoxyglucose is now in use and research with Gallium-68 is in progress with animal and in vitro studies ongoing. Also in progress is work with iodinated antibodies. Other new product involvement consists of those short-lived radionuclides (Na-24, K-42, Br-82) utilized in a total parenteral nutrition study under another investigator's protocol.

The radiopharmacy also provided a preceptorship for two students from Duquesne University School of Pharmacy Controlled Externship Program who are now pursuing graduate study in Radiopharmacy. In addition, two pharmacy students gained training and experience in the radiopharmacy

## Radiopharmaceutical Section (continued)

within the COSTEP. Lectures and consultative functions were also rendered to medical and paramedical personnel regarding various aspects of radiopharmacy.

## Whole Body Counter Section

During FY 81, the Section will be involved in a cooperative study with researchers at the University of Maryland to determine the feasibility of using stable isotopes of zinc, selenium and chromium to study trace metal metabolism and nutrition in infants and small children. These studies will use radioactive tracers and stable tracers simultaneously and the results will be compared with measurements in adult subjects. Stable tracer levels in blood and urine will be analyzed using neutron activation techniques, while levels of radioactive tracers will be measured with the use of gamma-ray spectroscopy techniques, as applied to other studies.

A new computer program was developed in FY 80 as part of the Section's cooperative effort with the Cardiology Branch, IR, NHLBI, to study tissue flow in canine myocardium using labeled microspheres. The new program provides an exact solution for six isotopes counted simultaneously in a single tissue sample. Development of the program required the solution of a 6x6 factor matrix and the development of serial program strings which utilized the entire capability of the Section's Wang 2200 computer system. This program has been implemented and is being used routinely for analysis of 6 isotope tissue samples.

# FUTURE OBJECTIVES TOWARD MEETING GOALS:

## Applied Physics Section

Clinical studies with the real-time cardiac imaging system will continue. Refinements of this system through appropriate software and hardware changes will also be continued. Collaborative animal studies (CB/NHLBI) will be continued.

The portable probe system will be further exploited in intervention studies in the Catheterization Laboratory and elsewhere. Investigations of the accuracy, precision, and assumptions underlying the scintigraphic method will be continued.

## Diagnostic Imaging Section

Departmental Research: New positron emitting radiopharmaceuticals are under development. The decision on whether NIH will acquire a cyclotron is still under consideration at the highest official levels. In the meantime the NRL cyclotron is being utilized.

Institutes and their branches are encouraged to utilize existing diagnostic techniques in their clinical research studies and to assist in the developm of new applications of existing tests as well as the development of new nuclear medicine tests.

## Radiopharmaceutical Section

The future objectives of the Section are to continue to collaborate with the service and research efforts of the Diagnostic Imaging Section and Clinical Center investigators involved in the formulation, development, and quality control of all radiopharmaceutical products intended for patient administration.

The projected utilization of positron emitting radionuclides will increase the radiopharmacy's duties in aspects pertaining to the chemistry and pharmaceutical quality control assurances of the labelled products.

## Whole Body Counter Section

Future objectives of the Section include continuing a program of expanding services to encompass an increasing range of research services, refinement of the Section's current support capabilities in the areas of human metabolism and nutrition, and the continuing development of clinical support for investigators who are presently unaware of the potential of whole body counting in their research programs.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 00007-04 NM |

PERIOD COVERED
October 1, 1979 through September 30, 1980

TITLE OF PROJECT (80 characters or less)

ECG-Gated Scintigraphic Angiocardiography

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | R.O. Bonow | Senior Investigator | CB NHLBI |
| | S.L. Bacharach | Physicist | NM CC |
| | M.V. Green | Chief, Applied Physics | NM CC |
| OTHER: | K.M. Kent | Senior Investigator | CB NHLBI |
| | J.J. Bailey | Head, LAS | LAS DCRT |
| | M.A. Douglas | Programmer | LAS DCRT |
| | H.G. Ostrow | Engineer | CSL DCRT |

COOPERATING UNITS (if any)

CB NHLBI
LAS DCRT
CSL DCRT

LAB/BRANCH
Department of Nuclear Medicine, CC

SECTION
Applied Physics Section

INSTITUTE AND LOCATION
Clinical Center, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

High temporal resolution ECG-gated scintigraphic angiocardiography (radionuclide cineangiography) is a computer-based, radiotracer imaging procedure that allows non-invasive visualization of the chambers of the working heart at rest, during bicycle exercise, during therapeutic intervention, etc. The procedure yields quantitative measures of left ventricular function such as ejection fraction, peak ejection rate, etc. Work is continuing to assess the accuracy of these data in man and to establish findings for the method in selected disease categories. Variations of this technique are being explored and will result in an inexpensive, portable device capable of continuous real-time measurement of left ventricular function.

PHS-6040
(Rev. 10-76)

## Project Description

### Objectives:

To continue to validate, develop and exploit ECG-gated scintigraphy (radionuclide cineangiography) and its variants in the detection, evaluation and quantitation of cardiac disease in man.

### Methods Employed:

Comparative clinical studies were continued during FY 80 (CB/NHLBI, APS) under the rest-exercise imaging protocol. Studies were continued to: (1) compare, in large patient populations, the sensitivity and specificity of radionuclide cineangiography with other established diagnostic procedures in the detection of coronary artery disease; (2) to ascertain the effects of surgical therapy on the exercise response of the left ventricle; (3) to ascertain the exercise response of the left ventricle following myocardial infarction; (4) to ascertain the effects of balloon dilation of the coronary arteries on ventricular performance; (5) to assess the exercise response of the ventricle to various medications and (6) to ascertain the effect of exercise on ventricular performance in the presence of other cardiac abnormalities.

Technical support of these efforts was continuous throughout FY 80 with some 800 patients being studied (APS). Scientific support for this project resulted in the implementation of a data base system to facilitate intercomparison of patient data. (APS). Scientific support continued toward development of reliable, fully automated data reduction algorithms and advanced display techniques for use in these cardiac studies. Several algorithms resulting from these investigations have been implemented in the real-time imaging system and are now being clinically tested (LAS/APS).

Basic investigations into the accuracy, precision and assumptions underlying these radionuclide studies were also continued during FY 80. Using an extremely high sensitivity scintillation probe, (CSL/APS) the time variation of left ventricular volume was measured with good precision during individual cardiac cycles (not heretofore possible). These data were used to directly verify the effects of gating these same data. We conclude that ECG gating introduces minimal error into these studies.

Investigations were also continued to evaluate several possible methods by which absolute ventricular volumes might be determined, a capability lacking at present.

Development and evaluation of a portable probe system were continued during FY 80. The present system is being used successfully in the catheterization laboratory to construct left ventricular pressure - volume loops in real time. This and other applications will be pursued in the forthcoming year.

Findings:

Representative scientific and clinical findings are detailed in the references.

Significance of the Research Program:

Radionuclide cineangiography is demonstrably useful in the detection and in the management of patients with cardiac disease. This procedure requires only an intravenous injection of radiotracer and is otherwise utterly non-invasive. It is rapid, safe, and can be repeated under varying circumstances such as exercise, medication, etc., for a period of hours, without further tracer administration. This characteristic also makes the technique suitable for continuous LV function monitoring. This application is being exploited through development of a portable probe system which will be employed in special measurement situations.

Proposed Course:

Continuation of the work.

Honors and Awards:

None.

Publications:

1. Bacharach, S.L., Green, M.V., Borer, J.B., et al: Instrumentation and data processing in cardiovascular nuclear medicine: evaluation of ventricular function. Seminars in Nuclear Medicine 9:257-274, October, 1979.

2. Leon, M.B., Borer, J.B., Bacharach, S.L., et al: Detection of early cardiac dysfunction in patients with severe BETA-THALASSEMIA and chronic iron overload. New England Journal of Medicine 301:1143-1148, November, 1979.

3. Bacharach, S.L., Green, M.V., Borer, J.B., et al: Beat-by-beat validation of ECG-gating. Journal of Nuclear Medicine 21:307-313, April, 1980.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 00007-06 NM |

PERIOD COVERED
July 1, 1979 to June 30, 1980

TITLE OF PROJECT (80 characters or less)

Radionuclide Cinepneumography

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

| | | | |
|---|---|---|---|
| PI: | B.R. Line | Staff Physician | NM CC |
| Other: | R.G. Crystal | Head, Pulmonary Branch | PB NHLBI |
| | B.A. Keogh | Chief, Clinical Service | PB NHLBI |
| | A.E. Jones | Asst. Chief, Nuclear Medicine | NM CC |
| | G.S. Johnston | Chief, Nuclear Medicine | NM CC |
| | S.L. Bacharach | Physicist | NM CC |

COOPERATING UNITS (if any)

PB NHLBI

LAB/BRANCH
Department of Nuclear Medicine, CC

SECTION
Diagnostic Imaging Section

INSTITUTE AND LOCATION
Clinical Center, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 3.0 | 1.5 | 1.5 |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Radionuclide Cinepneumography is a computer-assisted scintigraphic procedure that produces a series of images spanning an average respiratory cycle. The images allow quantitative assessments of the dynamics of regional pulmonary volume change and lung motion during resting tidal respiration, during bicycle exercise, and during theraputic intervention. Images are constructed from scintigraphic data with similar respiratory flow and volume characteristics so that they may be displayed in continuous-loop movie format. The technique is noninvasive and requires little patient cooperation or technologist time. Currently the procedure is under evaluation to determine its usefulness in improving the detection of pulmonary emboli, and in providing quantitative assessments of regional ventilation.

PHS-6040
(Rev. 10-76)

## Project Description

### Objectives:

To improve the clinical utility of Cinepneumography by reducing its technical requirements and computer analysis time.

To apply the noninvasive procedure to well defined patient populations to assess the cost-benefits of this new technology in sceening for pulmonary emboli and evaluating ventilatory dysfunction.

### Methods Employed:

Cinepneumography requires a computer and a gamma camera- devices common in Nuclear Medicine departments. In addition, an inexpensive air flow transducer, a pneumotachometer, is used to describe the patient's respiratory pattern. This is a short tubular chamber containing a low resistance grid which produces a measure of flow from the small pressure drop occuring across it during respiration. The scintigraphic proceedure is performed as usual; no other specialized techniques are required. As the pneumotachometer does not come in contact with the patient and produces an insignificant change in airflow resistance, it is totally non-invasive.

Scintigraphic image data and the pneumotachometer signal from 30-100 respiratory cycles are analyzed by the computer to produce a series of 12-60 images spanning a single average respiratory cycle. These images are quantitative descriptions of the regional tracer distribution during equal portions of the respiratory cycle. They may be used to quantitate the change in regional lung volume, timing of peak flow rates, and phase relationships of expansion in various portions of the lung.

Because the lung moves during respiration the images produced by standard scintigraphic techniques are blurred. Defects in ventilation or perfusion are smeared across the image and can be difficult to detect. The Cinepneumographic method produces a series of images, each representing the lung during a small phase of the cycle, so that the blurr in each is significantly reduced. In addition, these images may be displayed in rapid sequence, as a continuous-loop movie, so that the clinician may follow the change in lung shape and evaluate regional ventilation or perfusion abnormalities.

The technique is now being applied to evaluate regional perfusion during standard six-view lung scans requested to screen for pulmonary embolization. An upright exercise bicycle ergometer is being modified to study the changes in regional ventilation-perfusion during stress. Studies in collaboration with the Pulmonary Branch, NHLBI are being planned to assess the value of this new technology in following functional changes in patients with chronic lung disease.

## Findings:

The method and initial findings are detailed in the references.

## Significance of the Research Program:

Respiratory motion is well recognized as a factor degrading images of the lung, liver, spleen, and kidney. Quantitative phantom studies suggest that respiratory motion doubles the resolution distance for the imaging camera, and that clinicians using uncorrected images require 50% greater film-density contrast to detect a lesion 2 cm in diameter. Cinepneumography has been developed to reduce motion artifact and should thereby improve the clinical detection of defects in pulmonary perfusion associated with pulmonary emboli.

Ventilation assessments using radioactive Xenon require an analysis of the clearance of the tracer gas from the lung. This limits the assessment of regional ventilation to one view, and makes evaluation of ventilation during exercise or theraputic intervention very difficult. Cinepneumography is performed during equilibrium ventilation of the tracer gas. It can be repeated serially and in multiple views. This feature should improve the detection of regional ventilation-perfusion mismatch associated with pulmonary embolization and allow quantitative assessments of regional pulmonary function during stress and theraputic intervention.

## Proposed Course:

Continuation of the work.

## Honors and Awards:

Invited Lecture, Society of Nuclear Medicine, 1980 National Meeting: Ventilation-Perfusion Imaging for the Diagnosis of Pulmonary Embolism: A Current Prospectus.

## Publications:

Line BR, Cooper JA, Spicer KM, Jones AE, Crystal RG, Johnston GS: Radionuclide Cinepneumography: Flow-Volume Imaging of the Respiratory Cycle. J Nucl Med 21:219-224, 1980.

Alderson PO, Line BR: Scintigraphic Evaluation of Regional Pulmonary Ventilation. Sem Nucl Med 10:218-242, 1980.

## TABLE I

## Comparison of Whole Body Measurements for Fiscal Years 1979 and 1980

| | Isotope | 1979 | 1980* |
|---|---|---|---|
| **Research Studies** | | | |
| | Ca-47 | 11 | 0 |
| | Tc-99m | 0 | 97 |
| | Zn-65 | 3292 | 4186 |
| | Cr-51 | 108 | 0 |
| | K -40 | 166 | 117 |
| | I -131 | 1034 | 871 |
| | I-123 | 13 | 52 |
| | | 4624 | 5323 |
| **Personnel Monitoring Studies** | | | |
| | I-125, 131 | 1903 | 1498 |
| | Whole Body | 777 | 616 |
| | | 2680 | 2114 |

---

*Fiscal Year 1980 values estimated from 10/79 through 5/80 plus scheduled increases, expressed as yearly rates.

## TABLE II

## Other Analysis Related to Whole Body Metabolism Studies

| | FY 1979 | FY 1980 |
|---|---|---|
| Excreta Studies | | |
| Zn-65 | 1550 | 1036 |
| Cr-51 | 17 | 0 |
| | 1575 | 1036 |
| Blood Studies | | |
| Samples Taken | 1022 | 876 |
| Red Cell Washings | 1013 | 876 |
| | 2035 | 1752 |
| Blood Counts | | |
| Ca-47 | 9 | 0 |
| Zn-65 | 2026 | 1752 |
| | 2035 | 1752 |
| Tissue Sample Counting | | |
| Sr-85, Ce-144 | | |
| Yb-169, Sc-46 | 1254 | 4128 |
| Ga-67 | 76 | 0 |
| | 1330 | 4128 |
| Dose Calibrations | | |
| I-131 | 768 | 785 |

---

*Fiscal Year 1979 values estimated from 10/78 through 6/79 plus scheduled inceases expressed as yearly rates.

## TABLE III

### Twelve Year Record of Whole Body Measurements

| Year | Research Measurements | % of Total | Personnel Measurements | % of Total | Total Measurements | Yearly % Change | Yearly % Change from 1968 |
|---|---|---|---|---|---|---|---|
| 1968 | 1102 | 67 | 552 | 33 | 1654 | --- | --- |
| 1969 | 639 | 60 | 427 | 40 | 1066 | -36 | -36 |
| 1970 | 234 | 31 | 511 | 69 | 745 | -30 | -55 |
| 1971 | 317 | 36 | 566 | 64 | 883 | 19 | -47 |
| 1972 | 1168 | 71 | 476 | 29 | 1644 | 86 | - 0.6 |
| 1973 | 1863 | 64 | 1030 | 36 | 2893 | 76 | 75 |
| 1974 | 2138 | 68 | 1292 | 38 | 3430 | 19 | 107 |
| 1975 | 3615 | 68 | 1721 | 32 | 5336 | 56 | 223 |
| 1976 | 2311 | 52 | 2135 | 48 | 4446 | -18 | 163 |
| 1977 | 1485 | 44 | 1921 | 56 | 3406 | -23 | 106 |
| 1978 | 1670 | 39 | 2560 | 61 | 4230 | 24 | 156 |
| 1979 | 4624 | 63 | 2680 | 37 | 7304 | 73 | 342 |
| 1980* | 5323 | 72 | 2114 | 28 | 7437 | 2 | 350 |

---

*Fiscal Year 1980 values derived from 10/79 through 6/80 work load plus an estimation for 7/80 through 9/80.

## Table IV

## Radiopharmaceutical Section Statistical Data

| | FY-79 | *FY-80 | % Change |
|---|---|---|---|
| Service Requests | 1,948 | 2,192 | + 12.5% |
| Work Units | 22,999 | 28,512 | + 24.0% |
| Unit Dose Requests | 6,853 | 7,424 | + 8.3% |
| RPS Assays | 3,786 | 3,963 | + 4.7% |
| Radionuclidic Purity Checks | 531 | 527 | + 0 |
| RPS Expenditures | $118,142.90 | $107,092.23 | - 9.4 |

* FY 1980 = Projected Figure

## Table V

## Radionuclides and Products Received, Registered, and Formulated - FY 79

| | | | |
|---|---|---|---|
| 1. | H-3 | - | Dehydroepiandrosterone Sulfate<br>Glycerol<br>L-Phenylalanine<br>Testosterone<br>Water |
| 2. | C-14 | - | Dopa<br>Pentamethylmelamine |
| 3. | F-18 | - | 2-Fluorodeoxyglucose |
| 4. | Na-24 | - | Sodium Chloride |
| 5. | P-32 | - | Chromic Phosphate<br>Sodium Phosphate |
| 6. | K-42 | - | Potassium Chloride |
| 7. | Ca-47 | - | Calcium Chloride |
| 8. | Cr-51 | - | Chromic Chloride<br>Erythrocytes<br>Human Serum Albumin<br>Sodium Chromate |
| 9. | Co-57 | - | Cyanocobalamin Capsules |
| 10. | Co-58 | - | Cyanocobalamin Capsules |
| 11. | Fe-59 | - | Ferrous Citrate Plasma |
| 12. | Zn-65 | - | Zinc Chloride Plasma |
| 13. | Ga-67 | - | Gallium Citrate |
| 14. | Ga-68 | - | Gallium Chloride<br>Gallium EDTA<br>Gallium Ferric Chloride<br>Gallium Iron Dextran Colloid |

15. Se-75 - Selenomethionine

16. Br-82 - Ammonium Bromide

17. Mo-99 - Mo-99/Tc-99m Generator

18. Tc-99m - Antimony Trisulfide Colloid
    - Diethylenetriaminepentaacetic Acid
    - Macroaggregated Human Serum Albumin
    - Methylene Diphosphonate
    - Sodium Pertechnetate
    - Stannous Human Serum Albumin
    - Sulfur Colloid

19. In-111 - Diethylenetriaminepentaacetic Acid
    - Indium Chloride
    - 8-Hydroxyquinoline

20. I-123 - Sodium Iodide

21. I-125 - Alpha-1-Antitrypsin-M
    - C-II Apolipoprotein
    - Chylomicrons
    - Fibrinogen
    - Human Serum Albumin
    - Normal Apolipoprotein-E
    - Sodium Iodide
    - Type V Apolipoprotein-E
    - Very Low Density Lipoprotein

22. Xe-127 - Xenon Gas

23. I-131 - A-1 Apolipoprotein
    - Alpha-1-Antitrypsin-Z
    - Apolipoprotein-E
    - C-II Apolipoprotein
    - Sodium Iodide Oral Solution
    - Sodium Iodide Uptake Solution
    - Sodium-o-Iodohippurate
    - Type III Apolipoprotein-E
    - Type V apolipoprotein-E

24. Xe-133 - Xenon Gas

25. TI-201 - Thallous Chloride

## TABLE VI
## Diagnostic Nuclear Medicine Section

### Patient Visits by Fiscal Year

| Date | 1967 | 1968 | 1969 |
|---|---|---|---|
| Total | 2568 | 3093 | 1637 |
| Yearly % Change | | 20% | 47%* |
| Yearly % Change from 1967 | | 20% | 36%* |

| Date | 1970 | 1971 | 1972 |
|---|---|---|---|
| Total | 2181 | 2308 | 2950 |
| Yearly % Change | 33%* | 0% | 28% |
| Yearly % Change from 1967 | 15%* | 7%* | 15% |

| Date | 1973 | 1974 | 1975 |
|---|---|---|---|
| Total | 4688 | 7039 | 7098 |
| Yearly % Change | 59% | 50% | 0% |
| Yearly % change from 1967 | 82% | 174% | 176% |

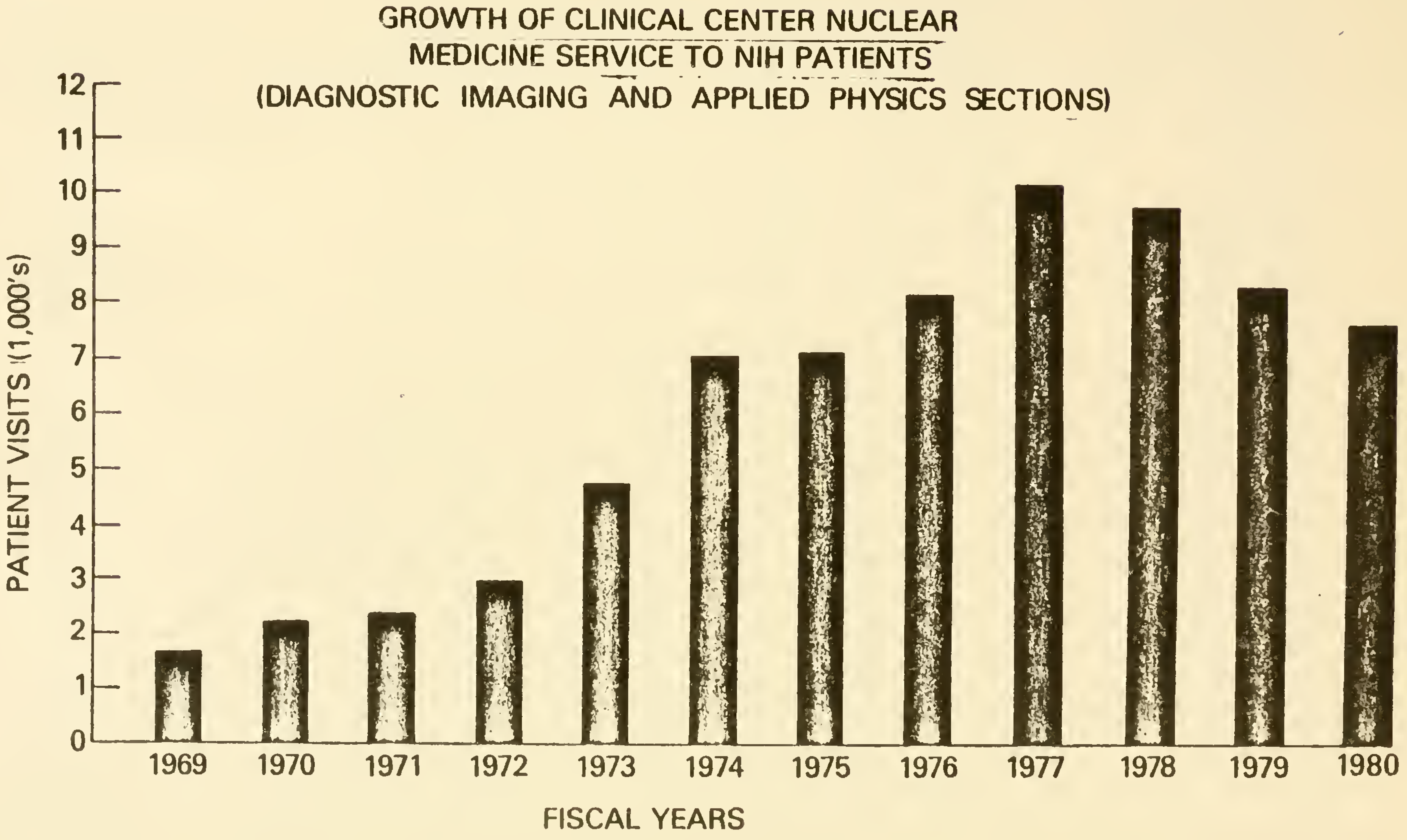
| Date | 1976 | 1977 | 1978 |
|---|---|---|---|
| Total | 8054 | 10056 | 9074 |
| Yearly % Change | 13% | 25% | 10%* |
| Yearly % Change from 1967 | 214% | 292% | 253% |

| Date | 1979 | 1980 |
|---|---|---|
| Total | 8200 | 7433 |
| Yearly % Change | 10%* | 10%* |
| Yearly % Change from 1967 | 219% | 189% |

---

* Decrease

1979/80 X-Ray Computerized Tomography Studies Transferred to X-Ray Department/CC



GROWTH OF CLINICAL CENTER NUCLEAR MEDICINE SERVICE TO NIH PATIENTS (DIAGNOSTIC IMAGING AND APPLIED PHYSICS SECTIONS)

October 1, 1979 through September 30, 1980

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

NURSING DEPARTMENT

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October 1, 1979 through September 30, 198(

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

NURSING DEPARTMENT

## I. Department Mission and Goals

The Nursing Department at the Clinical Center provides nursing services to patients and support to their families in a biomedical research environment. In addition to professionally identifiable nursing practices, the Nursing Department assumes the responsibility for many expanded nursing activities recognized as physician services by the Joint Physician-Nurse Committee of the NIH Medical Board. The implemented Nursing Department Philosophy and Goals (Attachments I and II) set the direction for the year. Annually each Nursing unit reviews its goals to meet the mission of the Department in keeping with this philosophy. In addition, each nurse in a major leadership role is required to develop individual goals assuring accountability for a major program area.

Goal achievement is monitored and recorded in the quarterly reports to Clinical Center Management and through biannual briefing sessions with the Chief and Deputy Chief of the Nursing Department. Significant accomplishments, problems and recommendations are addressed.

## II. Department Activities

A. The recruitment and retention of staff in sufficient numbers and level of competence to support the research and clinical activities of the Institutes remain a major activity. The Nursing Department faces a considerable challenge in recruiting professional nurses to achieve its research and patient care mission, 24 hours a day, seven days a week, within the constraints of a limited personnel ceiling, accreditation and nurse practice act requirements. In addition, the majority of the staff must be professional nurses because of the implementation of the primary nursing system, an innovation which is both attractive and satisfying to patients and staff. Interviews conducted with new head nurses after six months in their leadership roles indicated a strong desire for an all-professional staff with accountability and responsibility for its practice. To date the number of filled budgeted positions is 555 (Attachment III). Since January there has been a noticeable decline in the numbers and quality of professional nurse applicants, which reflects a national and regional nurse shortage. Civil service salaries are marginally competitive while community hospitals have become creative in marketing, offering comprehensive benefit packages. The general employment freeze has had a

negative impact on hiring, which interrupted recruiting efforts locally and nationally. Evaluation of present recruitment and retention activities, including intra- as well as extramural modalities, continues as a major endeavor.

B. Department reorganization efforts and creative management initiatives have further reduced the number of hours of overtime by 500 hours per quarter.

C. The retreat mechanism has continued to provide various organized groups within the Nursing Department an opportunity to evaluate group performance, to raise concerns, to solve problems, and to plan for the future. Accomplishments within each group have been significant.

The participating groups were:

Administrative Council
Head Nurses
Clinical Nurse Experts
Clinical Nurse Educators
Mental Health Nursing Service Leadership Group
Heart and Lung Nursing Leadership Group

D. Collaborative efforts with physicians and other Clinical Center departments have received extensive attention. They include a variety of modalities and approaches in an effort to maintain collegial working relationships, to facilitate and improve patient care, and support biomedical research. The modalities include, but are not limited to formal and informal meetings, teaching rounds, patient care conferences, and collaborative research.

E. "Talk to the Chief," informal 30 minute conferences on all tours of duty, were continued. Discussion focused on organizational changes, particularly those related to ambulatory care.

F. Nursing units 2B, 10N, 13W, and 6W implemented compressed work schedules. This pilot project will be reviewed in November for its effectiveness and popularity.

G. The administrative combination of the Eye, Arthritis and Metabolic, and Child Health Nursing Services under one service chief resulted in optimal uitilization of resources and increased staff satisfaction. Nursing Unit 12 East, with a majority of NICHD beds, was transferred to the Child Health Nursing Service in November for nursing administrative support.

H. The downgrading of the unit clerks posed a serious morale factor and is a source of deep concern. Proposed organizational changes should offer relief.

I. Meeting, classroom, and conference space has become increasingly scarce as renovations progress. Use of classrooms in Building 31

is extremely inconvenient and serves as a deterrent to staff participation in mandatory and continuing education offerings.

J. Staff nurses, through the Staff Nurse Advisory Committee, have become actively involved in identifying educational needs, developing program offerings, and participating in formulating different modalities for meeting their perceived needs. Liaison committees with head nurses, clinical nurse experts and clinical educators have been formed to develop mechanisms to achieve common goals.

K. Major refinements of the nursing content has been achieved with the implementations of the computerized MIS on all nursing units. The Discharge Nursing Care Plan is an official document in the Medical Record. The Discharge Summary, designed to facilitate care in the ambulatory setting, is in pilot stage on six nursing units.

L. Bylaws for the professional nursing staff have been developed and approved by the Administrative Council. Ratification procedure is yet to be determined.

M. With implementation of the total program of care concept and the return of one position to the NCI, support to patient care and research endeavors in the Pediatric Oncology Branch and Medical Oncology Clinics has been maintained by assessing clinic services and enhancing nursing knowledge and skills. Patients requiring care after regularly scheduled clinic hours are being seen on the appropriate nursing unit. A proposal has been submitted to the Joint Physician-Nurse Committee to prepare selected nurses to administer complex and toxic chemotherapeutic agents intravenously.

## III. Major Progress in Research, Services, Training, and Development

### A. Research

1. The Nursing Research Proposal Evaluation form has been re-written to follow the NIH proposal format. The policies for Nursing Research have been distributed to each unit as a section in the Nursing Administration Policy Manual.

2. The Sixth Annual Nursing Research Symposium in the Jack Masur Auditorium on April 8, 1980 was attended by approximately one hundred thirty-five people. Ms. Gayle Traver, R.N., M.S.N., Associate Professor, University of Arizona, spoke on the interdependence of nursing research and nursing practice.

3. Thirty-nine nurses, including nine non-Clinical Center nurses, attended a "Workshop for Nurses - Nursing Research Proposal Review" on January 8, 1980 and learned about the reviewer's role in nursing research proposal evaluation using established review guidelines.

4. Six nursing research proposals have been reviewed. One of the

proposals was developed and submitted by a student; the other five proposals were developed and submitted by Nursing Department members.

5. One doctoral candidate from the Catholic University of America is in the data-collecting phase of her study.

6. Ms. Marjorie Dehlinger, Head Nurse, 13N is associated with Dr. Griff Ross, Deputy Director, CC, in a study to determine the nurse's use of the computerized medical record. Findings from the study will provide the basis for a readily retrievable nursing data base.

B. Services to Patients

1. Modernization of the patient care units began this year with the movement of 2 West to 3 East and 3 East to 6D. Both moves could have benefited from greater coordination which would have considerably lessened disruption in delivery of patient care. Since completion of 13N, the patients on 13 East have been housed on that unit. A single laminar flow room has been completed on 2 East.

2. Four major organizational changes have taken place in the Nursing Department this year:

    a) A total program of care concept was implemented in February 1980. Service chiefs were given total responsibility and accountability for meeting the care and protocol requirements of patients wherever it was appropriate for them to be seen. Consequently, the Outpatient Nursing Service was abolished effective April 6, 1980. Staff were assigned to programs of care consonant with their knowledge and skills.

    b) Intense evaluation of the function of the evening/night supervisor's role began in November 1979. Collaborative effort with administrative services concerning non-nursing functions and support to the nursing staff resulted in the assignment of the six supervisors to the nursing services in a practice rather than administrative role. Service chiefs have 24-hour responsibility for administrative support in their individual programs. The 80 intermittent/part-time nursing staff assigned to the Central Nursing Office were reassigned on March 30, 1980, to the several nursing services. The reassignment was based on documented need and past practice.

    c) The position of Assistant Chief, Nursing Department became vacant with the assignment of Ms. Mary Rose Kennedy to CPOD, PHS, Rockville, Maryland. The position has been converted to one of practice.

d) Three nursing staff members of the MIS Cadre were reassign to nursing units as care givers November 1979.

3. A centralized cardio-pulmonary resuscitation team (CPR team) was implemented in November 1979. This team, consisting of coordinators from 6W and 7E, results in knowledgeable nurses responding to all arrests. Dr. Harry Keiser, Clinical Director, NHLBI coordinates all CPR activities for the Clinical Center.

4. JCAH reviewed the Clinical Center on October 15, 16, 17, 1979. The Nursing Department was well prepared for the visit and the recommendations for Nursing included: 1) review and approval of policies and procedures regarding the qualifications and employment of Nursing Department members; and 2) the written evaluation of the performance of nursing staff should be criterion-based and related to performance standards established by job description. A task force to develop the criteria is expected to have completed its charge by August 1980.

5. The medical intensive care unit, 10D, has been well-utilized by all the institutes. One hundred seventy-four patients have been admitted since June 30, 1979. Nurses assigned to 10D and 10N participated in a cross-orientation program to enhance their knowledge base and develop additional critical care skills.

C. Training and Development

1. The Central Nursing Office internship program has continued to prove effective in the development of professional nurses for leadership roles. Eleven nursing leaders and six staff nurses participated in the program this year.

2. In collaboration with the Career Development Branch, the first Nurse Career Development Plan baccalaureate nursing program begins with Georgetown University in July 1980. Ten candidates have been selected to enter the program this year through the competitive process.

3. Intramural programs for nursing staff have been developed including an intensive care nursing course, CPR training which provides certification by the American Heart Association, a preceptorship program for newly assigned staff, and the Professional Nurse series, developed in response to the Quality Assurance Evaluation. Blood and blood products and intravenous administration are now included in the orientation. The New Graduate Program provided twenty-eight nurses with planned support upon their entry into professional practice. New graduate turnover rate in 1980 was 11%; in 1979 it was 43%.

4. The total number of nursing employees oriented was 176 (Attachment IV).

5. Twenty educational programs were approved by the Public Health Service Review Committee on Continuing Education in Nursing (Attachment V).

6. In response to a major Clinical Center initiative, the program "Nurses' Responsibility and the Patient's Right to Know," was developed to enable nursing staff to be knowledgeable in assisting patients in viewing the Clinical Center film, "The Right to Know."

7. Affiliation with nearby universities continues to provide a viable modality for graduate students to utilize the resources of the Nursing Department during their clinical practicum. This year, four graduate students from the Catholic University and the University of Maryland have completed their work in this setting. In addition to the Chief Nurse, two clinical nurse experts (pediatrics) are faculty associates at the University of Maryland. The Assistant to the Chief, Nursing Department for Nursing Research holds an appointment as Adjunct Assistant Professor at the Catholic University.

8. In its fourth year, the Foreign Exchange Nurse Visitor Program in collaboration with the National Cancer Institute provided a six month exchange for a chemotherapy nurse from the Institut Jules Bordet, Brussels, Belgium. The second American nurse selected to participate in the program is from the Mary Hitchcock Memorial Hospital, Hanover, New Hampshire, and will be assigned to the Institut Jules Bordet.

9. The Nursing Department was represented at the annual intensive course in bioethics sponsored by the Kennedy Institute for Ethics at the Georgetown University by Ms. Janice Feldman, Chief, Child Health and Human Development Nursing Service and Jill Nusbaum, Head Nurse, Mental Health Nursing Service. A member of the Nursing Department is an active participant of the Agenda Organizing Committee on Bioethical Concerns of the Clinical Center.

10. Publications:

    Echelberger, C. "Care of the Heparin Lock," U.S. Department of Health, Education and Welfare, August 1979.

    Wachenhut, J.P. and Barnwell, R.A., "Burkitt's Lymphoma," AJN October 1979.

    Leon, M., Nonn, J., Bachrach, A., Green, M., Griffith, P., and Nienuis, A. Detection of Early Cardiac Dysfunction in Patients with Severe Beta-Thalassemia and Chronic Iron Overload, New England Journal of Medicine, November 22, 1979.

The following monographs of Clinical Conferences have been published:

Laminar Air Flow - Cancer Nursing Service

11. Significant Activities:

a) Ms. Vernice Ferguson, Chief, Nursing Department participated in:

Graduation, Pinning or Capping Ceremony Speaker (Nursing Programs) May-June at:

The University of the District of Columbia

The Maryland General Hospital School of Nursing at Baltimore

The University of Maryland School of Nursing at Baltimore

The Second Annual Soule Lecture - School of Nursing, University of Washington (Seattle)

Workshop leader - Third National Conference, Journal of Nursing Administration

Speaker - A.A.C.N. Conference on Masters Level Preparation for Nursing, Lexington, Kentucky

Workshop Participant - to review professional and general criteria for appointment of Army Nurse Corps officers in the Active Army and Reserve Components.

b) Ms. Ann McNemar, CNE, Child Health and Ms. Sue Simmons, CNE, Mental Health presented at the University of Maryland Conference on The Ethical Dimensions in Nursing Research.

c) Mrs. Catherine Gorrell, CNE, Central Nursing Office presented a paper entitled, "Frequency of Infections in Hospitalized Patients with Colon Cancer" at the Oncology Nursing Society Annual Meeting in San Diego, California in May 1980. Ms. Rosalie Smith, Ms. Audrey Barlock, and Ms. Claudia Seipp, Cancer Nursing Service, presided at round table discussions.

d) Ms. Jo Ann Alspach, CNE, Heart and Lung Nursing Service, has been appointed chairman of the Joint Physician-Nurse Committee to succeed Ms. Vernice Ferguson. Dr. Douglas Gasterland, NEI and Ms. Kathryn McKeon, Chief, Mental Health Nursing Service, have been selected to fill two other vacancies.

e) Mrs. Regina Dowling, Head Nurse, Plasmapheresis Laboratory presented a paper, "Applying the Nursing Process Within the Cytopheresis Setting" at the Society of Hemopheresis Specialists annual meeting. She was elected to serve a three year term on the SHS Board of Directors, serving as Chairman of the Continuing Education Committee.

f) Ms. Cheryl Yarboro and Mr. William Campbell, staff nurses on the Arthritis and Metabolic Nursing Service, presented a paper, "The Technique of Lymphocyte Depletion Via Aminco Continuous Blood Flow Cell Separator" at the National Meeting of the Society of Hemopheresis Specialist in New Orleans.

g) Ms. Linda McNeely presented, "Computers in Nursing-A User's Perspective," at the TRIMIS Conference on "The State of the Art with Computers in Nursing," held at Walter Reed Medical Center April 28, 1980.

h) Bernice Crossley and Karma Harmon presented "Computers in Clinical Medicine: A Nursing Perspective of MIS" at the Clinical Center.

i) Ms. Donna Putt, CNE and Shirley Bruce, staff nurse, Eye Nursing Service, presented a paper entitled, "Drugs in Ocular Therapy," on November 6, 1979 at the National ASORN Meeting in San Francisco.

j) Ms. Janice Feldman, Chief, Arthritis and Metabolic Nursing Service, participated in a forum on the needs for arthritis-related research and education of nursing. The purpose of the forum was to assist the National Arthritis Advisory Board in formulating recommendations to Congress and to the Department of Health and Human Services.

k) The first Nursing Departmental Awards were presented at the sixth Annual Program Meeting of the Nursing Department. The annual program in October featured Madeleine Leininger, R.N., Ph.D. and Arthur Levine, M.D. on the topic, "Change." Ms. Vernice Ferguson, Chief, Nursing Department received the Nursing Department's first Distinguished Nurse Award, and Ms. Juliana Rugg, R.N., the first Nurse of the Year Award.

l) Ms. Jo Ann Alspach, CNE, Heart and Lung Nursing Service, has been appointed a member of the board of directors of the American Association of Critical Care Nurses.

m) Kathleen McCormick, R.N., Ph.D., Assistant to the Chief for Nursing Research, has been elected to the Executive Committee, Council of Nursing Research, American Nurses' Association.

n) Ms. Venida Hamilton and Ms. Barbara Scott are members of the NIH Women's Advisory Committee.

o) Mrs. Venida Hamilton, Clinical Nurse Educator, is Vice-President of the District of Columbia Nurses' Association.

12. Significant Personnel Changes

a) Ms. Vernice Ferguson, Chief of the Nursing Department of the Clinical Center resigned effective July 12, 1980 to become Chief, Nursing Service, Veterans Administration. Mrs. Janice Feldman, Chief, Eye, Arthritis and Metabolic Diseases and Child Health and Human Development Nursing Services is a member of the multi-disciplinary Search Committee seeking a new Chief for the department.

b) Mr. Max Gearhart, former Chief, Mental Health Nursing Service, has taken a position as Clinical Educator at the PHS Hospital, Indian Health Service, Shiprock, New Mexico. Ms. Kathryn McKeon has been appointed Chief, Mental Health Nursing Service.

c) Ms. Virginia Dodds has resigned as Chief, Heart and Lung Nursing Service. Ms. Freddie Grice has been appointed acting Chief of the Service.

d) Ms. Catherine Gorrell, Clinical Nurse Expert assigned to the Central Nursing Office in September 1979, has clinical responsibility in NCI radiation clinic for patients on the breast cancer protocol, and serves as a resource to the Ambulatory Nursing Care Co-ordinators.

e) Ms. Barbara Brugliera, Nursing Coordinator for Professional Service, accepted a position as Deputy Chief, Division of Federal Employee Occupational Health, effective July 1, 1980.

f) Mrs. Emma Vogel has been reassigned from the Outpatient Nursing Service to be the second Assistant Chief, Cancer Nursing Service.

## IV. Future Objectives Directed Toward Meeting Goals

At the annual retreat of the Nursing Department's Administrative Council in January 1980, the following goals and plans for action were formulated:

1. Critical care initiatives designed to meet the immediate needs of the Department and future programs involving affiliation with a university and philanthropic organization.

2. Ambulatory care reorganization based on a total program of care concept.

3. Quality Assurance program, collectively developed and mutually agreed upon, to be implemented and maintained at the level of the nursing service with accountability and authority for its maintenance vested in the service chief.

## Clinical Center Nursing Department
## Philosophy

The Nursing Department of the Clinical Center is committed to supporting biomedical research through the provision of nursing care for patients and the support of their families and/or significant others. Our major goal is to provide individualized nursing service, utilizing Primary Nursing, which is consonant with the wide range of health-care requirements of patients in this setting.

Professional nursing at the Clinical Center is defined as encompassing practice, administration, education, and research. Nursing is a clinical practice discipline. The nurse is responsible and accountable for utilizing the nursing process to assist the patient to achieve optimum health goals, or when a return to health is not possible to set new goals and initiate appropriate nursing action. Patients and those most closely involved with them should be active participants in the formulation and attainment of realistic health goals.

In nursing practice, we function both independently and interdependently. When meeting patient-care needs requiring nursing judgment, we function independently; when these needs require the involvement of others, we function collaboratively.

The goal of nursing administration, education and research is directed toward the continual improvement of nursing practice. We foster an environment in which staff members can acquire knowledge, increase clinical skills, demonstrate leadership, and participate in nursing research in order to establish a position of pre-eminence for professional nursing practice. We provide an environment which facilitates students' learning experiences.

Members of the Nursing Department adhere to a code of ethics. We are accountable for our actions to recipients of services for providing safe and competent care, to peers and the professional nursing community for setting and maintaining acceptable standards of care, to the institution for working in accord with organizational goals, and to the community-at-large for improving and contributing to the health care delivery system.

For Nursing Department Manuals

Formulation Date------------------April, 1979------------------

Implementation Date--------------June, 1979--------------------

Review Date-----------------------January, 1980-----------------

ATTACHMENT I

## CLINICAL CENTER

## NURSING DEPARTMENT GOALS

The mission of the Nursing Department is to support biomedical research through the provision of humanistic and theory-based nursing care, care for patients, and support to their families or significant others. To accomplish this mission the goals follow:

1. To have accountable, ethical, documented nursing PRACTICE.
2. To have nursing SERVICES SUPPORT which facilitates nursing practice.
3. To have nursing EDUCATIONAL PROGRAMS which augment nursing practice.
4. To have a nursing RESEARCH PROGRAM which improves patient care.
5. To occupy a local, national, and international position of preeminence in nursing.

FORMULATED: 4/79
IMPLEMENTED: 6/79
REVIEWED: 1/80

ATTACHMENT II

## ATTACHMENT III

## STAFFING DATA - NURSING DEPARTMENT

| | June 30, 1979 | June 30, 1980 |
|---|---|---|
| Total number of positions | 593 | 555 ** |
| Total number of positions filled | 607 | 557 |
| Total number of vacancies | +14 | +2 |
| Administrative | | |
| Total number of positions | 59 | 49 |
| Total number of positions filled | 54 | 44 |
| Total number of vacancies | -5 | -5 |
| Clinical Instructors | | |
| Total number of positions | 8 | 6 |
| Total number of positions filled | 7 | 7 |
| Total number vacancies | -1 | +1 |
| Nurse Clinicians | | |
| Total number of positions | 30 | 39 *** |
| Total number of positions filled | 27 | 38 |
| Total number of vacancies | -3 | -1 |
| Staff Nurse | | |
| Total number of positions | 351 | 338 |
| Total number of positions filled | 382 | 349 |
| Total number of vacancies | +31 | +11 |
| Practical Nurse | | |
| Total number of positions | 24 | 23 |
| Total number of positions filled | 26 | 25 |
| Total number of vacancies | +2 | +2 |
| Technical Positions | | |
| Total number of positions | 10 | 1 |
| Total number of positions filled | 10 | 1 |
| Total number of vacancies | 0 | 0 |
| Nursing Assistants | | |
| Total number of positions | 61 | 56 |
| Total number of positions filled | 61 * | 54 |
| Total number of vacancies | 0 | -2 |
| Clerical | | |
| Total number of positions | 50 | 43 |
| Total number of positions filled | 40 | 39 |
| Total number of vacancies | -10 | -4 |

*Includes 2 students in Stride Nursing Program at Marymount.

**Indicates transfer of 39 positions to the Surgical Services Dept. 7/15/79.

***Includes 6 E/N Supervisors converted to CNE's 6/1/80.

## ATTACHMENT IV

Annual Report, July, 1979 through June 30, 1980
page 5 continued

Employees oriented - 176

| | | |
|---|---|---|
| 03 | Commissioned Officer | 2 |
| 02 | Commissioned Officer | 2 |
| 01 | Commissioned Officer | 6 |
| GS - 11 | Clinical Nurse Educator | 1 |
| GS - 11 | Clinical Nurse Expert | 4 |
| GS - 11 | Supervisory Clinical Nurse | 1 |
| GS - 9 | Clinical Nurse | 81 |
| GS - 9 | Clinical Nurse (Part-Time) | 4 |
| GS - 7 | Clinical Nurse | 23 |
| GS - 7 | Clinical Nurse (Part-Time | 1 |
| GS - 5 | Nurse (Transfer from Stride) | 1 |
| GS - 4 | Nurse (Transfer from Stride) | 1 |
| GS - 4 | Nursing Assistant | 2 |
| GS - 4 | Nursing Assistant (Summer) | 4 |
| GS - 4 | Nursing Assistant (Cancer Work Study) | 20 |
| GS - 3 | Nursing Assistant (Summer) | 1 |
| GS - 4 | Clerk-Typist | 16 |
| GS - 4 | Clerk-Typist (Summer) | 1 |
| GS - 3 | Clerk-Typist | 3 |
| GS - 3 | Clerk-Typist (Summer) | 1 |
| GS - 2 | Clerk-Typist (Summer) | 1 |

## ATTACHMENT V

National Institutes of Health
Clinical Center
Nursing Department
Nursing Education

Continuing Education Programs in Nursing Approved by the Public Health Service Review Committee on Continuing Education in Nursing

| | TITLE | CONTINUING EDUCATION UNIT |
|---|---|---|
| A. | Cancer Nursing - '79 | 0.15 |
| B. | Computer Training for Nurses Module VI | .4 |
| C. | Fifth Annual Nursing Research Symposium "Stress Reduction Through Patient Education" | .2 |
| D. | Group Theory and Process | 1.6 |
| E. | Health Education: An Essential Component of Health Care | 0.1 |
| F. | Nephrology Nursing Course - Level I | 2.0 |
| G. | Nephrology Nursing Workshop - Level II | .6 |
| H. | Neurological Assessment for Nurses | .7 |
| I. | Nursing Care Responsibilities for Patient's Receiving Blood and Blood Products | 1.6 |
| J. | Nursing Care of the Patient with Thalassemia and Iron Overload | .15 |
| K. | Nursing Management of the Patient on the MAI Ventilator | .2 |
| L. | Nursing Research Proposal Review Workshop | .6 |
| M. | Preceptorship and Perspective in Role Clarification | 0.2 |
| N. | The Primary Nurse Role and The Nursing Process | 1.0 |
| O. | Primary Nursing in an Ambulatory Setting | .15 |
| P. | Respiratory Assessment | 2.8 |

| | TITLE | CONTINUING EDUCATION UNIT |
|---|---|---|
| Q. | Rheumatoid Arthritis | 0.2 |
| R. | Seventh Nursing Forum: Current Issues in Nursing Co-Sponsored by Office of Chief Nurse, USPHS and Nursing Department, Clinical Center | .4 |
| S. | Sixth Annual Program Meeting "Change" | .1 |
| T. | Sixth Nursing Forum "Hospice" Co-Sponsored by Office of Chief Nurse, USPHS and Nursing Department, Clinical Center | .2 |
| U. | Suicide - The Challenge For Nurses | 0.2 |

10 contact hours=1 continuing education unit
June 1980

October 1, 1979, through September 30, 1980

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

# SUMMARY OF ANNUAL REPORT OF PROGRAM ACTIVITIES
# CLINICAL CENTER

## NUTRITION DEPARTMENT

### CONTENTS

Department Mission and Goals . . . . . . . . . . . . . . . . . . . . . . . . Nt-1
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October 1, 1979, through September 30, 1980

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

## NUTRITION DEPARTMENT

### I. DEPARTMENT MISSION AND GOALS

In a total research hospital such as the Clinical Center the Nutrition Department's role is a unique one for it must not only assume the usual responsibilities of a hospital food service organization but must also take an active role in all research programs in a supportive manner. Because of the exacting requirements of its program, the Nutrition Department cannot delegate part of the patient food service to another service as is done in other hospitals, but assumes full responsibility for the entire operation.

The Nutrition Department's contribution to the research program involves the control of patients' dietary intake as ordered by research investigators. The Department assumes the responsibility for precise and complete intake data. In addition, the Department provides nutritional instruction to inpatients when there is a need for exact follow-through on the specific dietary requirements during the time of their hospitalization. On occasion, such instructions involve times when patients are on pass (1-10 days).

Outpatient instruction is given to facilitate the implementation of certain protocols or as a follow-up of studies that were initiated as inpatient protocols. As needed, nutrition histories are taken to determine whether or not a patient will be suitable for a given protocol.

Decentralized food service is utilized throughout the house which involves food being prepared in one central kitchen and individual trays being served in one of 12 floor kitchen units. The use of decentralized tray

service provides a valuable means of meeting an individual patient's needs and preferences as well as the nutritional research needs of the investigators.

Two specialized kitchen units, the 8th Floor Metabolic Kitchen Unit and the 2B Laminar Flow Unit, have been in continuous operation this year. The Metabolic Unit provides investigators from NHLBI, NIAMDD, NCI, and NICHD with services that permit them to undertake metabolic balance studies and other carefully controlled studies involving the measurement of nutrient intake. The food and food service the Laminar Flow Unit provides is uniquely designed to control and reduce the high risk of infection by providing a protected environment for patients undergoing chemotherapy.

The Nutrition Department's continued support of research programs through diet therapy provides an integral part of medical care to assist the physician in treating a specific disease or in helping the patient adjust to a disease or post-surgical condition. Individually-calculated diets were provided to meet physicians' orders and patients' food preferences. These diets were as time consuming and in many cases as complicated as those which were directly related to research studies.

## II. DEPARTMENT ACTIVITIES

During Fiscal Year 1980 the Nutrition Department served a total of 320,848 meals. Of these, 103, 014 were classified as Category 3 and 4 tyoe diets. These categories required professional staff participation in planning individual meals and service which are an integral part of a clinical research study and provide the investigator with necessary nutritional information to assist with the interpretation of the data obtained. Many of the clinical research protocols implemented at the Clinical Center necessitated the control of nutrients, total calories, fluids, and in some cases the control of source

of supply of food served. Well-qualified staff in sufficient numbers are essential to the success of these programs.

## III. MAJOR PROGRESS IN RESEARCH, SERVICES, TRAINING AND DEVELOPMENT

Approximately 32% of the total meals served in this fiscal year were directly related to medical research at the Clinical Center. In addition to serving three meals a day, the Nutrition Department has provided these additional services:

1. Measured and controlled fluids in conjunction with the nursing staff on an average of 53-66 per day.
2. Provided an accurate measurement of all food eaten for an average of 35-40 patients per day. (This required measuring all food served and returned and a daily calculation of nutrient consumption.)
3. Provided a control of specific nutrient intakes for approximately 67-88 patients each day. (This required checking back each meal tray and replacement of the appropriate nutrient being controlled by nutrient intake.
4. Responded to an average of 134-197 dietary changes per day.
5. Provided an average of 361-389 diet instructions and/or consultations per month to the clinical studies being followed on an outpatient basis.

Nutrition expertise has been provided to the NIH Nutrition Coordinating Committee, the NIH GAO Investigation of food service to cancer patients at selected hospitals. In addition, nutrition expertise has been provided to a number of private hospitals in the United States and individual dietitians.

Considerable time has been devoted to purchasing demands, marketing changes, and to the NIH Office of Financial Management in the handling of payment for purchases received. The market changes and procedural changes

at NIH has added considerably to the workload in each of these units.

Emphasis has been placed on improvement of communications within the Nutrition Department and with other departments of the Clinical Center. The Nutrition/Nursing Committee has worked together over the past year to simplify the procedure used for fluid intakes and procedures for developing guidelines for diet ordering through the MIS. The quantity of food items presently ordered daily by each head nurse is being reviewed by the Nutrition/Nursing Committee.

Work has been undertaken this year to initiate and implement a centralized tray service for the total Clinical Center possibly in October of 1981. Several different systems of centralized tray service have been evaluated and recommendations have been made for changes to be implemented.

There has been continued emphasis on training for all groups within the Department. Colonel Thelma Arnold, Assistant Professor of Biochemistry, USUHS, has continued to serve as a consultant to the staff of the Patient Dietetic Service. Since October 1979, she has spent two days each month in this capacity. In addition, with Dr. Ned H. Kalin, the senior investigator, and Colonel Thelma Arnold as a co-investigator, the Nutrition Department has undertaken a nutritional status study in conjunction with NIMH patients on long term care studies here at the Clinical Center. To help implement this study, the Nutrition Department accepted Ensign Sandra Yerkes, senior medical student, for a four-month clinical elective in nutrition under the immediate supervision of Colonel Thelma Arnold. Arrangements were made for Ensign Yerkes to work with dietitians serving in other Institutes to observe nutritional care of patients.

## IV. FUTURE OBJECTIVES DIRECTED TOWARD MEETING GOALS

During the year the Nutrition Department Goals Committee established

seven major goals. Some have been completed and others have been partially developed. These are:

1. Develop new menus to reduce the number to a three-week cycle. All menus, charts to tally each day's menus, and purchasing plans were completed; the new plan was initiated on September 29, 1980.
2. Plan an orientation for each staff member to review plans for handling a fire in the Clinical Center. These training sessions were held on June 10 and 12, 1980.
3. Revise the Portion Manual - A college student (dietetics major) is assisting with this project. About 50% is completed.
4. Develop guidelines for ordering diets and communicating appropriate information between medical and nursing staff and the Nutrition Department. The guidelines covered communications through the MIS as well as hand-written and verbal communications.
5. Revise the Diet Manual by preparing two parts:
    A. A Procedure Manual for physicians and nurses to be completed in June 1981.
    B. A Diet Manual describing diets in general use at the Clinical Center ( to be revised by June 1982 ).
6. Establish a procedure for documenting nutritional care for all patients to be initiated in October 1980.
7. Document a plan to identify quality assurance for nutritional care at the Clinical Center.

## V. PROBLEMS

The major problem of the Nutrition Department continues to center around the failure of the contractor (employed to remodel the Main Kitchen in July 1975 ) to complete the contract agreement. Work was begun on this

remodeling in November 1975. At the end of Fiscal Year 1980, 50% of the work has been accomplished. This delay has placed an unnecessary burden on the Food Production Service staff and has contributed to poor morale, absentee problems, an increase in accidents, and in some cases the reduced quality of food served to the patients.

Increased accident rates in the Department and difficulties in employing individuals to fill vacancies has necessitated a number of adjustments in Department procedures. Inflation continues to influence increases in cost of food, supplies, and equipment. Lack of allocated funds to replace equipment and to initiate purchasing requisitions and the extended length of time it takes to have paperwork processed through the Procurement Office has handicapped all units throughout the year.

Inflation and the necessity of having to pay a considerable amount of overtime has caused increased expenditures as indicated below:

| | | |
|---|---|---|
| FY 1980: | Personnel | $3,415,569 |
| | Food | 758,817 |
| | Equipment and Supplies | 10,856 |
| | Other Costs | 215,145 |
| | | $4,400,387 |

October 1, 1979, through September 30, 1980

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

OFFICE OF OCCUPATIONAL MEDICINE

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October 1, 1979, through September 30, 1980

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

## OFFICE OF OCCUPATIONAL MEDICINE

### Department Missions and Goals

The Office of Occupational Medicine through the Occupational Medical Service provides an extensive medical program for all employees of the National Institutes of Health which includes all elements of the Federal Employee Occupational Health Program as specified by Executive and DHHS Directives.

The Occupational Medical Service is administratively accountable to the Chief, Office of Occupational Medicine, CC, who also serves as the Occupational Health Officer, NIH. National Health Services, Inc., was selected through competitive bidding as the contractor for the operation of the Occupational Medical Service at NIH beginning July 1, 1974. In carrying out its responsibilities, the Occupational Medical Service works closely with the Director, Division of Safety, Office of Research Services, and NIH Institute Clinical Directors.

The Occupational Medical Service is responsible for maintaining essential services and facilities to provide emergency treatment for on-the-job illness or injury of employees; provides health education and preventive medical programs to make employees aware of the importance of maintaining good health; advises management and employees in resolving work-related health problems; assists management in evaluating handicapped individuals in terms of specific job assignments; develops and executes a comprehensive mental health program for NIH, including alcoholism and drug abuse counseling,and develops medical surveillance programs designed to minimize environmental health hazards.

The Occupational Medical Service's goal is to assure that employees are able to perform their duties without hazard to themselves or others; to offer job assignments in relation to medical fitness; to provide preventive medical services to assist employees in meeting their health needs; to prevent adverse effects of hazards in the work environment; and to provide clinical consultation for occupational diseases for employees and Clinical Center patients at the request of Institute physicians.

### Department Activities

#### A. Workload

Statistics in Table I have been prepared for October 1, 1979, through September 30, 1980. Statistics used for the last quarter of FY-80 are those from the last quarter of FY-79, since statistics for the end of FY-80 are not yet available. There has been an increase in the total number of visits in comparison to last year's report.

### B. Personnel

In December 1979 the position of Director of CPR Training was created by abolishing a vacant registered nurse position.

### C. Physical Plant and Equipment

Modifications in the main Health Unit included sound-proofing the offices for the psychiatrist and the mental health counselors and construction of a new reception desk-counter. Three new examining tables were added to the physicians offices, doubling the capacity to do physical examinations. A new spirometer with a microprecessor and surplus slit lamp with applanation tonometer were also added to the main Health Unit.

### D. Administrative Items

The semi-annual meeting of the Operations Research Advisory Committee was held September 6, 1979. Subjects discussed included: Asbestos Medical Surveillance Protocol, Policemen Physical Examination Protocol, Computer Medical Surveillance Scheduling, Employee Assistance Program, Cardiopulmonary Resuscitation, and a Review of OMS Goals and Objectives. A significant recommendation from the Committee was the establishment of a position in OMS for a CPR Coordinator to continue the successful program developed by the Chief Nurse. In October 1979 the OMS Medical Director met individually with members of the Operations Research Advisory Committee to answer specific questions regarding OMS on-going programs. A simil meeting was held with Ms. Badger, CC Administrative Officer, and the NIH Occupational Health Officer on September 27, 1979.

Dr. Winter, Chairman of the Board, EHE/NHS and Dr. Wanago visited NIH on September 20 and met with the NIH Occupational Health Officer and the Operations Research Advisory Committee to review contract performance. As a result of this visit OMS was reorganized, making the Assistant Medical Director responsible for the day-to-day operation of the clinic and supervision of key personnel. The duties of the Medical Director were broadened to include wider interaction with NIH management and safety personnel and expansion of OMS medical surveillance programs.

The OMS Medical Director presented the annual review of OMS programs to the Clinical Center Director and the Administrative Officer for the NHS/NIH contract on October 2, 1979. This meeting was attended by the OMS Assistant Medical Director and NIH Occupational Health Officer. As a result of this presentation a decision was made to add the position of CPR Coordinator to the OMS staff.

The revision of the OMS Procedures Manual, started in January 1979, was completed in September. The Manual has about 600 pages and major changes included the addition of a Table of Contents, numbering of the pages, a page to record changes, and several new sections. Eight changes to the OMS Procedures Manual were published February 28, 1980. These changes are part of the periodic updating of this Manual.

The OMS Employees Information Brochure was revised in September and 10,000 copies were ordered. This brochure is distributed to new employees during their pre-employment examination and to personnel officers. About 3600 copies were mailed directly to supervisors. It will also be placed on several racks used at NIH for educational material.

On October 3, 1979, the OMS Medical Director was invited by the NIH Equal Employment Opportunity Council to make a presentation about the NIH/NHS contract operations. This meeting was attended by the NIH Occupational Health Officer and the OMS Chief Mental Health Counselor.

The March 18, 1980 issue of the NIH Record publicized the need for volunteers to participate in studies of the diagnostic effectiveness of allergy extracts conducted by the FDA Bureau of Biologics. As in previous years, OMS made the main Health Unit available for skin testing and administration of desensitization agents. This year the Building 13 Health Unit was also used for this project.

On November 20, 1979 an open house was held at the Federal Building Health Unit for employees of the Federal, Landow, and Del Ray Buildings to acquaint them with the various programs of OMS. The OMS Assistant Medical Director was present to answer questions from employees.

At the request of the staff nurse, the triage system was discontinued because the services of the triage nurses were not felt to be contributing sufficiently to maintain adequate patient flow. In addition, this system did not work well in the physical layout of the temporary main Health Unit.

In an effort to improve services to employees in the Westwood Building, a meeting was held with management and labor representatives and it was agreed to expand the Employees Assistance Program and to initiate allergy injections service at Westwood. A physician is present at this building for two hours a week for allergy injections.

## Major Progress in Research, Services, Training, and Development

### A. OMS/Division of Safety Liaison Meeting

Following the NIH reorganization of the Safety Office these montly meetings replaced the former OMS/Environmental Safety Branch Liaison Meetings. In the January meeting, Dr. Wanner, Deputy Director, Division of Safety, described the new organization and their operating procedures. The placement of the Division of Safety at the NIH Director's level indicates a new awareness at NIH for Occupational Safety and Health Programs. New and revised medical surveillance programs were coordinated with this group.

### B. Medical Surveillance

New medical surveillance programs for employees potentially exposed to substances requiring periodic health monitoring included: lasers, ethylene oxide, polychlorinated biphenyls, Q Fever, and asbestos. Programs revised and updated included: animal handlers, autopsy assistants, tetrachloro-

ethylene, hepatitis-B, and insecticides. A medical and psychiatric examination protocol was developed for the newly established position of policemen. In contrast to NIH guards these individuals will be carrying firearms. Slit lamp examinations were given to laser workers and glass blowers. The medical surveillance program for individuals working with chemical carcinogens will be expanded to comply with new Occupational Safety and Health Act guidelines.

### Computer Medical Surveillance Program

The purpose of this new program is to develop a master list of employees in surveillance programs according to Institutes or Divisions, job titles, types of surveillance, and dates of recall. In addition to the master list, a monthly list will be printed listing those employees due in a particular month. Additions, deletions, or other changes will be made periodically to maintain the program up-to-date.

### Special Virus Containment Program (SVCP)

In May 1980 the Assistant Medical Director completed the second draft of the health record review of this eight-year-old program. Findings and recommendations were presented at a Division of Safety/OMS meeting May 15, 1980. Dr. A. Hellman who is in charge of this program at NCI notified the group that on October 1, 1980, supervision of this program was the responsibility of the Division of Safety. Dr. R. Wanner, Deputy Director Division of Safety will organize a working group to expand the SVCP pr gram to other NIH workers who are potentially exposed to chemical carcinogens.

## C. Clinical Center Safety Committee

Needle Stick Sub-Committee. An OMS staff nurse attended two meetings of this Sub-Committee and presented statistics on needle stick injuries. Recommendations of this Sub-Committee included better use and labeling of disposal containers and an educational compaign on the proper disposal of needles. At the request of OMS, the NIH Safety Office agreed to expand this safety program to all NIH Institutes and Divisions.

Ethylene Oxide Sub-Committee. This Committee met February 11, 1980 to review the planned surveillance program for ethylene oxide workers. Following this meeting the OMS Medical Director prepared the final draft of this surveillance protocol.

Clinical Center Infection Control Committee. In preparation for the JCHA visit to the Clinical Center, OMS staff revised and submitted for approval to this Committee infection control policies used at OMS. The Medical Director provided advice to the Committee Chairman regarding the revision of the hepatitis-B surveillance program.

D. NIH Biosafety Committee. The Medical Director participated in a subcommittee which met with the NIH Occupational Health Officer to make r commendations to the Institutes Scientific Directors to use OMS for their

serum bank collection and to share results of their employees' serum titer studies with OMS.

E. Biological Safety Conference. The OMS Medical Director presented the paper "Occupational Medical Program and Medical Surveillance at a Bio-medical Facility" at the 22nd Biological Safety Conference, attended by about 140 biological safety officers from Government, academia, and private industry.

F. Community Activities in Occupational Medicine. On March 27, 1980, the OMS Medical Director was invited to a meeting at Johns Hopkins School of Public Health and Hygiene to plan a regional collaboration effort for improvement of occupational health programs in teaching and research medical centers in the Baltimore-Washington area. Centers included in this effort are: Georgetown University, George Washington University, Howard University, University of Maryland, Johns Hopkins University, the Uniformed Services University of Health Sciences, USPHS Hospital, Baltimore, Md., and the National Institutes of Health. Bi-monthly meetings of program directors were planned and meetings have already been held at NIH and Johns Hopkins University. OMS provided technical assistance and sample medical surveillance protocols to the Smithsonian InstiututION and the Uniformed Services University of the Health Science for the development of medical surveillance programs.

The OMS Medical Director is a member of the ad hoc Committee on Occupational Lung Disease, Lung Association of Mid-Maryland and the D. C. Medical Society Committee on Environmental and Occupational Health.

G. Employee Assistance Program. The Employee Assistance Program, developed and expanded from the Alcoholism and Drug Abuse Program, continues to expand its services. New programs implemented during this year included: (a) Overater Annonymous weekly meetings, (b) a five week training program in "Effective Communication, (c) a three part series of workshops on "Dealing with Teenagers" and, (d) Psychiatric in-service sessions for staff counselors every other week to provide peer review, utilizing the staff psychiatrist, Medical Director, and Assistant Medical Director. On-going programs include: (a) two weekly Alcoholic Annonymous meetings; (b) weekly Alanon meetings; (c) bi-weekly therapy group for alcoholics; (d) five week American Cancer Society Smoking Cessation Program; (e) sessions on "Stress Reduction in the Workplace"; (f) group consultation with nursing staff from several oncology wards; (g) Employee Assistance Program "Awareness Sessions for Supervisors." In the "Conflict and Cooperation Study" of February 1980, prepared for NIH by the Organizational Psychology Research Unit of the Office of Personnel Management, the Employee Assistance Program received the highest rating on the question concerning conflict resolution. This was in comparison to the other formal conflict resolution mechanisms which are the EEO Discrimination Process Complaints, the Grievance Process, and Personnel and Guidance Counseling.

H. Employee Health Education. This is a very active program at NIH, and some of its significant accomplishments included multiple presentations of the following educational programs and/or movies: "The Later Years" - psychological implications of the aging process and retirement, "Romance to

Recovery" - effects of alcoholism on the family, "Sense in the Sun" - prevention of skin cancer, "Health Fraud Rackets" - quackery methods of health promotion, "Breast Self Examination" - a cancer detection program and, "Look Before You Eat" - basic good nutrition. The OMS staff psychiatrist presented a course for supervisors entitled "Understanding Employee's Problems." The OMS Medical Director and the staff mental health counselors made presentations in the course "Introduction to Supervisors", presented by the Executive and Management Branch, Division of Personnel Management. The mental health counselors participated in a training seminar on "Conflict and Agreement" presented by OMS and the Division of Personnel Management and made numerous presentations describing their services and creating an awareness of their programs.

Summer students were addressed on the subject of "Alcoholism and Drug Abuse". The chief mental health counselor also addressed the NIH Equal Employment Opportunity Council to explain the Employee Assistance Program. As a result of this presentation the Medical Director addressed the Council on OMS programs. The Medical Director gave the presentation "Continuing Programs and New Initiatives in OMS" to the CC Director and Department Heads, NIH Intramural Research Administrative Officers, CC Nursing Department Administrative Council and CC Patient Activities Department.

I. Cardio-Pulmonary Resuscitation. The Coordinator for CPR Training organized a pyramid program of CPR training for NIH employees, expanding the existing CPR program at OMS and developing an in-house pool of instructors. The instructors will be asked to teach a class twice a year. Additional CPR manikins were ordered and a space remodeled in Building 13 for a classroom. The movie "A Life in Your Hands" was shown as a motivational aid to encourage NIH employees to learn CPR. Twelve presentations were made throughout NIH and outlying buildings and the CPR Coordinator was present to answer questions and enroll employees in CPR courses. Since its inception, OMS trained 434 employees in CPR. Thirty-two employees were trained as instructors. All OMS clinical personnel received refresher training and recertification in CPR. The CPR Coordinator is preparing a CPR training pamphlet for NIH employees. The Clinical Center and the National Heart, Lung and Blood Institute are providing assistance in the preparation of this publication. The NHLBI Information Office will publish this pamphlet and develop a promotion and distribution plan.

J. Staff In-Service and Out-Service Education and Training. The Chief Mental Health Counselor attended the following courses or conferences: A six day course in "Diagnostic Assessment and Treatment Planning" at Catholic University; the American Psychological Association Annual Convention, a two-day Conference on Women and Acloholism, presentations on "Crisis Intervention" and "Depression"; and the meeting of the Association of Labor-Management Administrators and Consultants on Alcoholism (ALMACA). The staff mental health counselor is enrolled in a part-time graduate social work program at Catholic University. In their efforts to familiarize themselves with local referral resources, the mental health counselors visited several treatment and rehabilitation centers in the local area.

The Chief Nurse and a staff nurse attended a workshop entitled "Hypertension - Update for Nurses." The CPR Coordinator and the Chief Nurse attended the first annual Maryland State Workshop for CPR Instructor Trainers sponsored by the American Heart Association Maryland Affiliate. The Chief Nurse also attended a course in "Physical Assessment of the Adult Patient", sponsored by American University and Lucy Webb Hayes School of Nursing and the American Occupational Health Conference. Two regular staff nurses and a per diem nurse are attending a course in "Physical Assessment of the Adult Patient", sponsored by Montgomery College.

In-service training for the nursing staff and health technicians included the following subjects: Comprehensive review of cardiac emergency drugs; establishing and maintaining a life line, intravenous fluids,and the addition of medications; cardiac arrest mock drills; assessment and treatment of upper respiratory problems; oxygen and inhalation therapy, use of nebulizer, and bag resuscitation; review of transportation of non-ambulatory patients to Building 10 for X-ray or physiotherapy; proper completion of medical records in cases of occupational injuries or diseases and compensation forms and procedures; review of emergency room equipment, medications, and procedures; alcoholism effect on the family; and CPR recertification. An occupational health technician and the Building 13 Health Unit nurse attended an Occupational Hearing Conservation Program offered by the Washington Hearing and Speech Society at Sibley Memorial Hospital. They were certified as Occupational Hearing Conservationists.

Physicians' participation in continuing education included attendance at the following courses and/or meetings: Graduate Courses in Toxicology and Internal Medicine Review Courses at the Graduate School (FAES); Annual American Occupational Health Conference; Quarterly Meetings of the National Capital American Occupational Medical Association; American College of Chest Physicians Conference on Hypertension and a course in Office Evaluation of Allergies; University of Maryland Conference on Antibiotics in the Compromised Host; monthly meetings of the D.C. Medical Society Committee on Environmental and Occupational Health' course in Industrial Medicine at the annual meeting of the Puerto Rico Medical Association; NIH Conference on Prevention of Hepatitis-B, and Seminar on Health Effects of Energy Conservation Related to Indoor Environment. The staff Psychiatrist attended the course "Comprehensive Review of Neurology" at Georgetown University. She attended this course in preparation for her Board examinations in April 1980, when she was certified by the American Board of Psychiatry and Neurology. The Assistant Medical Director was certified in General Preventive Medicine by the American Board of Preventive Medicine in December 1979.

## Future Objectives Directed Towards Meeting Goals

OMS future objectives include the formation of a Program Planning and Development Advisory Committee, formerly identified as the Operations Research Advisory Committee. This new Committee will be formed by the NIH Occupational Health Officer to assist in the development of explicit methodology for identifying priorities for program planning and development activities with OMS. At the end of the first three months of the new contract the contractor will present preliminary drafts for a minimum of 15 proposed studies as a basis for their

program planning and development. The Committee will select 10 subjects from which the contractor will present detailed protocols in March 1981 when priorities and projected dates of completion will be determined. OMS future objectives to continue to meet NIH needs will depend on the priorities set by the Committee.

In June 1978 OMS main Health Unit was temporarily moved from the Clinical Center Building 10, to Building 31 due to the construction of the Ambulatory Care Research Facility (ACRF). OMS plans call for the relocation of the main Health Unit to the sixth floor of the ACRF. A better layout of examination rooms and reception/waiting area will improve the flow of patients and reduce waiting time at the clinic. OMS staff have sorely missed the day-to-day contact with the various supporting clinical services such as X-ray, laboratory, and other consulting services. Improvements in OMS services will result from this move.

## SELECTED WORKLOAD STATISTICS

| | Number of Visits | | Average Monthly Frequency | | Precent of Workload | |
|---|---|---|---|---|---|---|
| | FY-79 | FY-80 | FY-79 | FY-80 | FY-79 | FY-80 |
| Preventive Medicine Visits | 24,307* | 26,663** | 2,026 | 2,222 | 65 | 66 |
| Personal Visits | 8,373 | 8,551 | 698 | 713 | 22 | 21 |
| Occupational Injuries | 3,156 | 3,234 | 263 | 270 | 9 | 8 |
| Occupational Diseases | 1,577 | 1,727 | 131 | 144 | 4 | 5 |
| Total Visits | 37,413 | 40,245 | 3,118 | 3,348 | 100 | 100 |

* Includes 1800 visits for Employee Assistance Program

** Includes 3060 visits for Employee Assistance Program

October 1, 1979, through September 30, 1980

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

# SUMMARY OF ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICALCENTER

## OUTPATIENT DEPARTMENT

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PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

# SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
# CLINICAL CENTER

## OUTPATIENT DEPARTMENT

### PROGRAM OBJECTIVES

The mission of the Outpatient Department is to assist the Clinical Center staff to provide excellence in patient care. The Department's goal is to provide effective and convenient settings, and expeditious and comprehensive service to Clinical Center patients.

The Outpatient Department is made of six sections: Admissions, the Clinics, the Patient Travel Office; Special Ambulatory Care Program; Local Transportation; and the Messenger and Escort Service. Each section provides special services to meet specific kinds of patient needs.

The following are the individual objectives for each section, and all, acting together, meet the overall objectives of the Department.

Admissions - The objective of this section is to admit both the inpatient and the outpatient in the most expeditious manner possible, ensuring that all information received and transcribed is accurate.

The Clinics - This section provides a setting in which physicians are able to conduct examinations and/or treatments of ambulatory patients on a timely basis, with assistance from other members of the Clinical Center staff.

The Patient Travel Office - This section provides and arranges transportation to and from the Clinical Center, taking into consideration the patients' medical and personal needs, comfort, and care with the least inconvenience to the patients.

Special Ambulatory Care Program - The objectives of this program is to offer participating Institutes and physicians a method of treating ambulatory patients, not living within commuting distance, on an outpatient basis. The patients are housed in a nearby motel and provided transportation to and from the Clinical Center for treatment.

Local Transportation - The objective of this section is to provide essential transportation for patients when the patient cannot provide his own. This includes transportation to and from the air, train, and bus terminals, special care and driver service for debilitated patients, and ambulance service for those patients needing more technical care.

## DEPARTMENT ACTIVITIES

The following departmental activities are designed to meet the overall objectives of the Department as well as those of the individual sections to provide the support necessary for the highest quality patient care:

1. To maintain the maximum productivity of the employees within the Department.

2. To hire a Chief, Clinics Section, of the Outpatient Department.

3. To review the operations of the Outpatient Department in light of the impact of the Ambulatory Care Research Facility which will be operational in FY 81.

4. To train the staff through various educational programs to improve efficiency and efficacy.

5. To continue to improve the supply system for the Clinics.

6. To review the various transportation contracts to ensure not only compliance, but also their cost effectiveness without diminishing patient care.

7. To orient Institute physicians to the Outpatient Department.

8. To implement the Medical Information System into the Clinics section.

9. To work with the Nursing Department's Ambulatory Care Coordinators in the Clinics to assist their effectiveness in their relationships with patients, physicians, and other Clinical Center departments and staff.

10. To work with the Admissions section and Institute physicans and staff to improve the communication between them.

11. To effectively reduce the money spent on travel and the Special Ambulatory Care Program without curtailing patient care.

12. To begin to plan for the relocation of the clinics into the ACRF.

13. To begin to order the necessary medical equipment for the ACRF.

14. To work with the Nursing staff to improve the Messenger and Escort Service to their various units.

15. To continue to increase the number of patients who are pre-admitted to the Clinical Center so that the patients spend less time in the Admissions Office.

16. To continue to improve the Travel Office's services to the patients through an expanded and improved computerized system, and further cut down on costs.

17. To work more closely with ancillary services personnel in order to solve mutual problems and expedite patient studies and result returns.

PROGRESS ACHIEVED

1. Some of the training programs to improve the output of work of the various employees of the Department are: inservice training sessions, participative management, and individual counseling sessions. This process is an indefinite one, as it is difficult to place limitations on it if it is to be successful.

2. The new Chief, Clinic Section, Mr. Howard R. Frank, began work with the Department on June 16, 1980.

3. An Outpatient Department Committee was formed to review current operations within the clinics and to assimilate data on time spent by the patients in the clinics and ancillary services. The committee has made several recommendations concerning the reorganization of the present Outpatient Department. The study concerning the length of time outpatients stay within the building for a clinic visit was completed by the end of August.

4. Various training courses were received by staff. The Medical Clerks underwent a six week condensed course in medical terminology so they could more effectively transfer physicians' orders into the Medical Information System. A number of persons have attended the Communications Workshop, the Assertive Approach course, and the Human Relations course.

5. The Clinic Supply System continues to improve. Close work with the Pharmacy Department has helped develop drug formularies for all Clinics.

6. The various transportation modes were reviewed throughout the year. The limousine service from National Airport has been most effective; however, there were not enough patients coming into Dulles to make the service cost effective. Having three taxi companies service our local patient area has been very efficient, as well as less costly.

7. The physicians of the various Institutes were oriented by the supervisors of the Special Ambulatory Care Program, Patient Travel, Admissions Section and Clinics. This is an ongoing program for all new Clinical Center Associates. In addition to orienting the new Clinical Associates, contacts were made with Clinical Directors to inform them of changes made within the Outpatient Department, and to keep them abreast of new developments.

8. The Medical Information System (MIS) was implemented into the Outpatient Department on June 9, 1980, beginning with Dental Consults and expanding to Diagnostic Radiology and Diagnostic Imaging, with the ancillary services included in September. The Medical Clerks and staff of Office of Communications and Management Systems have worked together in order to solve the many problems relating to the MIS, as it relates to outpatients. The Department has had an overall smooth transition onto MIS. The OPD MIS Computer Manual has been formulated and is helpful to the users.

9. The Outpatient Nursing Service was abolished on April 11, 1980, and the system of Institute Ambulatory Care Coordinators was established. Much work has been completed with the Ambulatory Care Coordinators in order that they can better assist the patient, physician, and other Clinical Center departments and staff. The reorganization, and opening of the ACRF in the near future has required that policies and procedures be updated and new ones established. Both of these activities will continue for the next year.

10. Communication between the Admissions Section and Institute physicians has been much improved throughout the year. The physicians are becoming more aware of the admitting process, both on an inpatient and outpatient basis.

11. The Institutes are looking closely at their expenditure of monies for Travel and the Special Ambulatory Care Program. We have been assisting them by suggesting ways to reduce these expenditures.

12. Plans for the relocation of the clinics into the Ambulatory Care Research Facility are being prepared. We have worked with the Institutes' Clinical Directors in formulating these plans. Statistics have been made available to better enable them to project their needs for the ACRF. This will be an ongoing process until the move is completed.

13. Ordering of all Clinic equipment for the ACRF has been completed.

14. Meetings have been held with nursing staff in order to work out problems with the Messenger and Escort Service. A better understanding now exists between the two disciplines.

15. The number of patients who are not being pre-admitted is diminishing as a result of better communications and better understanding on the part of the physicians on the importance of preadmitting the patient, which reduces the time the patient spends in the Admissions Office.

16. The Travel Office continued to improve its services to our patients and employees. Various computerized accounting systems for the Travel Office have been studied and one has been chosen.

17. Contacts and communications with Outpatient Department staff and the ancillary services have improved greatly over the past year, which has greatly enhanced the care for our patients.

## OTHER ACTIVITIES

1. The Chief, Outpatient Department is a member of the OPD MIS Committee which meets weekly to discuss problems of, and plans for, the MIS.

2. The Chief, Outpatient Department, started a committee with the Medical Clerks of the Clinic Section and members of the Office of Communications and Management Systems to discuss problems they were having with MIS. This committee meets on a weekly basis.

3. The Chief, Outpatient Department, is on the Medical Records Subcommittee on Forms and Systems, which meets monthly.

4. The Chief, Outpatient Department, is the chairperson of the Disaster Committee, a subcommittee of the Safety Committee. This committee is re-evaluating the Disaster Manual for the hospital.

5. The Chief, Outpatient Department, meets on a monthly basis with the employees of the various sections which comprise the Outpatient Department.

## PLANS

1. To continue to train employees of the Outpatient Department in public relations and other related areas.

2. To continue to define and refine the Outpatient Department program for stocking the Clinics.

3. To continue to work with the Institute Ambulatory Care Coordinators of the Nursing Department.

4. To continue to work on the Outpatient MIS implementation.

5. To continue to work on the relocations plans for the Ambulatory Care Research Facility.

6. To develop policies and procedures regarding the Ambulatory Care Research Facility and the Central Research Service Center.

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SUMMARY OF ANNUAL REPORT OF PROGRAM ACTIVITIES
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PATIENT ACTIVITIES DEPARTMENT

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PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

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CLINICAL CENTER

## PATIENT ACTIVITIES DEPARTMENT

### I. DEPARTMENT MISSIONS AND GOALS

This year the primary mission of the Patient Activities Department was to provide a diversified, patient-centered program of therapeutic recreation activities and library services to all patients of the Clinical Center, both in-and outpatients. These programs were designed to meet the physical and psychological needs, interests, and capabilities of Clinical Center patients and to be consistent with medical research objectives. Department goals included:

the education or re-education of the patient in the constructive use of his leisure during hospitalization and after discharge

the elimination of boredom, and as a result, to help alleviate stress and anxiety

the introduction of a variety of new recreation and cultural opportunities to the patient

the support needed to help the patient regain or reinforce his self esteem

the provision of emotional and psychological support to the patient and his family

the adaptation of leisure activities for the patient, based on his physical and emotional needs and on his individual research protocol

the continuation, as much as possible, of the patient's normal leisure activities during periods of hospitalization

All programs were organized, executed, and evaluated under the guidance of a professional staff of therapeutic recreation specialists and assistants.

### II. DEPARTMENT ACTIVITIES

### A. Therapeutic Recreation Section

1. Adult Recreation Referral Program
Based upon a written referral from the attending physican, this program featured creative arts and crafts, and sports. This year of the 2414 patients referred to the particular program, 2078 (approximately 86%) participated. For a more detailed statistical breakdown, see Attachment #1, Item #1.

As part of this program, 172 different patients were worked with on their units on a one-to-one basis.

2. Adult Social Program
   a. Clinical Center Program - This program featured seasonal events, dances, musical programs, trips, feature films, and many other appropriate social activities. This year, there were 312 activities planned, with 11,218 patient/family participants.

   b. Bedside Visitations (Medical Intensive Care Unit, 13 West and general Therapeutic Recreation Referrals)
   This year, 66 patients were assessed and worked with on a one-to-one basis.

   c. Semi-Ambulatory Care Program - Recreation activities were offered to patients and family members at the United Inn. This year there were 78 activities planned, with 920 patient/family participants.

3. Children's Play Programs (All Institutes)
   A creative and diversified play program was offered to all child patients, siblings, and child visitors. Activities were held predominantly in the 14th Floor Playroom. This year, 1139 different child patients and child visitors were involved in the program. For a more detailed statistical breakdown, see Attachment #1, Item #2. As part of this program 66 different child patients required bedside visitations.

4. Institute Programs: Therapeutic recreation activities were geared to meet specific patient/Institute needs in FY80.
   a. Mental Health Programs (3 East & West, 4 East & West, 6D)
   700 patients were involved in this program. For a more detailed statistical breakdown, see Attachment #1, Item #3.

   b. Pediatric Oncology Program
   Units 2E/2B: There were 732 patients on these units, with 38 confined to the Laminar Flow Rooms.

   OPD - West Clinic: There were 1201 outpatients and 2560 patient visits to this Clinic; in addition, 250 siblings visited the Clinic.

   c. Adult Cancer Program (10 East, 12 East & West, 13 East)
   2308 patients were involved in these programs. For a more detailed statistical breakdown, see Attachment #1, Item #4.

   d. Neurology Program: 999 patients were involved in this program.

   e. Heart Program: 953 patients were involved in this program and were worked with on a one-to-one basis.

   f. Child Health Program: 388 patients were involved in this program, receiving a variety of recreation services.

## B. Patient's Library Section

### 1. Books

| | |
|---|---|
| Inventory | 6910 |
| New Acquisitions | 357 |
| Lost in circulation | 61 |
| Discarded | 379 |
| Circulation (patients & personnel) | 10437 |
| via Library | 7490 |
| via Bookcarts | 2923 |
| Inter-library loan | 24 |
| Outpatients | 362 |

### 2. Patients Contacted

| | |
|---|---|
| Visiting Library | 6447 |
| Visited on Unit (bookcart) | 8195 |
| Outpatients | 2320 |

### 3. Magazines

| | |
|---|---|
| Subscriptions | |
| Monthly | 41 |
| Semi-monthly | 2 |
| Bi-monthly | 3 |
| Bi-weekly | 5 |
| Weekly | 22 |
| Quarterly | 1 |
| Circulation (Inpatients/Outpatients) | 10628 |

### 4. Newspapers

| | |
|---|---|
| Subscriptions | |
| Washington Post | 28 |
| Wall Street Journal | 1 |
| Christian Science Monitor | 1 |
| Circulation (Washington Post) | 10192 |

5. Reading Utilization - see Attachment #2

## III. MAJOR PROGRESS IN SERVICES/TRAINING/DEVELOPMENT

### A. Patient Library Section

During the past year, the Patient's Library experienced an increase in the number of inpatients and outpatients using this service. The library staff provided full service to Clinical Center patients. The bookcart, stocked with the most current books and magazines, was brought to each unit once every week, and any special request made by a patient or by staff member on behalf of a patient was given priority attention.

Mrs. Swim, Library Supervisor, continued to be an integral part of the 2 West Mental Health interdisciplinary team, giving the children on that unit extra reading time. She was required to evaluate the specific patient behavior in relation to the type or quality of drug intake. She worked with three children per week for about two hours each. There was a total of 20 different child patients involved in this program for an average stay of fifteen weeks.

As a result of a study started in January 1980 to determine how we could better serve the outpatients, we now take the bookcart to the East and South Clinics every day with a selection of magazines and paperbacks for the patients. There is also a large variety of hardback books which patients can charge out if they plan to return within a month. We are having a favorable response to this service.

## B. Therapeutic Recreation Section

### 1. Programs

a. Mental Health Program (Units 3E/W, 4E/W, 6D)
The professionals in this program exhibited a considerable effort to increase their staff development and career involvement over the past year. Many of the staff with minimal funding support attended one or more training sessions, conferences, or workshops to extend their professional expertise.

Ms. Patti Tepsic, TRS, co-authored a research paper with investigators in Child Psychiatry, entitled, "Hyperactive Children on Dextroamphetamine During Active Gym Program," to appear in The Psychobiology of Childhood: Profile of Current Issues. This paper is also appearing in Psychiatry Research Journal, in print Summer, 1980. These publications represent a "first" for our Department in collaboration with researchers at the NIH. Ms. Tepsic received a special Cash Award in recognition for her work on this research publication.

The Mental Health program saw several innovative changes and revisions in the past year: relaxation techniques, ballet classes, creative exploration hour, combining Art Therapy and Recreation Therapy, and a within section staff development meeting held on a monthly basis. The "total mental health" concept of staffing has created considerable stress on staff who were already functioning with 55 man hours less to provide services for their patients. These stresses signaled a change in program philosophy, and a request for an outside consultant has been submitted.

b. Adult Cancer Program (Units 10E, 12E/W, 13E)
The major achievement in this program over the past year was a greater professional acceptance of our program by the medical personnel, particularly the nurses; they seemed more aware of the need for, and value of, recreation for their patients. As a result, more unit coverage and activities were requested and initiated. The NCI Surgery, Medicine, and Radiation Branch Clinics

also asked for coverage; however, time and staffing did not allow us to accommodate this request.

Some of the added activities for this program include: off-reservation trips and weekly craft workshops. These workshops (leather/macrame/dried flower arranging/silk flowers) were held in the 10 East Solarium or at the patient's bedside.

A major success story was a Christmas decorating party on the 10 East Nursing Unit. With the help of nursing personnel and volunteers from the unit and Intensive Care, forty patients and their guests decorated the floor to perfection. The finale of the evening was decorating the tree with spray snow. The nursing staff from 10 East brought all of the bedridden patients out to the solarium, and around the tree. On the count of three, every patient in bed sprayed snow at the tree and each other! This was the highlight of the year.

c. Heart Program (Units 6W/7E)
The Recreation Therapist, being an integral member of the research team, stimulated staff and patient interest in, and a greater awareness of, our program. As a result, we received more requests for services to the pre-op and post-op patients. Based upon time and staffing, we were able to accommodate these patients on a limited basis.

Over the past six months, new medical research studies involving surgery were introduced, bringing in more patients. These new studies required 80% of the patients on 7E to be confined to the unit. This, along with the regular physician's rotation (every three months), fostered a great deal of stress and anxiety on both patients and staff alike. Our program definitely helped minimize these problems.

During the past year, we had patients from five different countries, who spoke only their native tongue. This proved to be a tremendous problem, for we are all dedicated to the philosophy of service to all patients; it is difficult, though not impossible, to service those with whom you cannot verbally communicate.

For the first time this year, two Therapeutic Recreation Interns rotated through this program and chose to spend a portion of their "concentrated time" on these units; they contributed greatly by enabling more "one-to-one" contact with the patients and their families.

d. Semi-Ambulatory Care Program (United Inn): After almost a year's hiatus, our recreation program in this area was re-instated. Assigning a part-time Recreation Assistant to plan programs for this population added a new dimension to the patients' stay at the Motel. Activities included: trips into the community, num ous social and special events, and creative craft workshops. These

activities gave these patients and their families an opportunity to socialize with each other and, more importantly, to relieve the stress and strain of their medical treatment. Thus far, the program has been well received.

e. Pediatric Oncology Program (Units 2E/2B & West Clinic)
In preparation for the move into the ACRF, several of the Clinic nurses were rotated from Units 2E/2B and the West Clinic in an effort to provide continuity between the two areas. This situation was extremely difficult at first for all staff, as well as patients, and caused a great deal of disruption in everyone's communication and interpersonal relations.

A memo was sent to Dr. John Zeigler, Associate Director, Clinical Oncology Program, Division of Cancer Treatment, NCI, regarding the need for POB playroom space in the ACRF; he was most supportive of our request.

Our recreation program in the Clinic might conceivably be expanding to encompass an internship program for students who are interested in learning about the "Child Life" aspects of a pediatric oncology recreation program. We are awaiting further clarification and instructions from the educational agency seeking our support.

"Interdisciplinary Approach: Fact or Fantasy?," National Conference of the Association for the Care of Children in Hospitals, Dallas, Texas, July, 1980. This was a paper written by eight authors from NIH, among whom were Joanie Hussey and Janis Partin of the therapeutic recreation staff. The paper was presented in Dallas, Texas by only two of the eight authors (one of whom was Janis Partin) since funding was unavailable for all eight. A workshop followed the presentation. Publication is being considered by the authors in various professional journals.

f. Child Health Program (Unit 9D & 11E)
Our involvement in Unit 9D and 11E included participation in the weekly interdisciplinary meeting, plus programming for all patients housed on these units. Although this program is classified as "pediatric,", the age range fluctuated weekly from infant to young adult; this made programming for this unit difficult - "flexibility" was the activity motto. Also, the very limited recreation space on the unit was adequate for the younger patients, but did not afford room for the older kids. As a result, off-unit activities were stressed; these included: ski trip to Altoona, Pa., ventures to the YMCA for swimming, bowling, and movie and theatre trips into the community. It should be noted that the medical staff (doctors/nurses) were most supportive of all our programs.

g. New Programs
A "first" for our Therapeutic Recreation Program was the administrative clearance to take two unusual trips. One was a skiing venture to Altoona, Pa. (February 1980) for a select group of obese adoles-

cents from Unit 9D; the other was an overnight camping trip to Prince William Forest, Quantico, Va.(July 1980) for twelve mental health patients and accompanying staff. These trips would not have been as successful as they were if it had not been for the hard work of our staff and the total support and cooperation we received from Nursing and Nutrition. We hope and plan to move ahead and have more of these trips.

2. Other

a. Staffing

With the loss of our two part-time permanent slots in the Mental Health Therapeutic Recreation Program in FY80, the staff faced a crisis: it was necessary to realign staffing to meet some of the recreation needs and demands of the patients on the "abandoned Units." Thus, Ms. Cindy White, Therapeutic Recreation Specialist, was assigned, part-time, to cover Unit 6D and, at the same time, continue her programming responsibilities on Neurology (5E/5W). After a brief "settling-in" period, programming in both areas (Neurology & Mental Health) reached an acceptable, though minimal, level of coverage. In the past, we have provided a comprehensive Recreation Therapy program on all five NIMH Units, including evening and weekend activities. Presently, the existing staff shortage has greatly impaired our former level of functioning.

b. Renovation - 14th Floor Gymnasium

Due to renovation of the gymnasium supposed to take 30 days but lasting 6 1/2 months, all programs usually held in this area, and the bulk of its equipment, were transferred to the 14th Floor Assembly Hall. The move was most traumatic for patients and staff alike. However, once we adjusted to the move, the transition was a good one, and we encountered few serious problems. We have now moved back into the newly renovated gym. The bright colors and new lights have helped stimulate patient participation in our arts & crafts and sports program, giving the patients a feeling of cheerfulness and comfort. We have received many compliments from patients, guests, and staff as to the brightness and vitality of this area; everyone is most pleased. This is the first renovation of this area since the Clinical Center was opened.

c. Staff Development

In late April and early May, a three-part series of staff development sessions were held to help ascertain staff attitudes toward their job. Prior to these meetings, staff had the opportunity to submit personal, programmatical, and professional "concerns" for consideration at these sessions. The end result from these various "concerns" submitted was the topic, "Lack of Professional Self-Image." Ms. Anne Proctor, Educational Services Officer, CC, was invited to sit in on the first two sessions as an objective observer. After consultation with the Department Chief, Ms. Proctor held a session with the staff, asking them for solutions to the main issues. Their recommendations were: 1) provide a mandatory orientation program for staff; 2) establish a staff development

program. Accordingly, a Staff Orientation Committee and a Staff Development Committee were established and given deadlines (July and August 1980) for their initial written proposals. We are hoping that everything we have experienced will help strengthen departmental communications and effectiveness.

d. Committee on Adolescents
A social work/nursing committee investigated the social, recreational, psychological, and physical needs of our adolescent patients. As a result, a committee was formed to address these needs. Charles Butler, Supervisor, Children's Therapeutic Recreation Program, agreed to co-chair this committee, along with June McCalla of Nursing. Others from our Department on the committee are Joanie Hussey, Janis Partin, Holly Anderson, and Arnold Sperling. Committee goals are: 1) presentation of an educational symposium on the hospitalized adolescent; 2) more structured and diversified leisure programs for the adolescent. Thus far, a Teen Group was formed, which meets Monday and Wednesday evenings on the 14th Floor, and plans were put in motion for the symposium presentation. Response from CC supportive staffs to this committee has been most favorable.

e. Newcomer's Guide
A patient handbook of fun, food, and facts was created by Sue O'Connell of our staff. It is a guide of the Bethesda area and includes places to eat, shopping, sightseeing, movie houses, etc. The guide is distributed to all patients, especially those in the SACP. It has proven to be a most useful and popular booklet! (See Attachment #3).

f. Patient Christmas Committee
The success of our Patient Christmas Program was not solely ours. The Patient Christmas Committee, made up of representatives from Nursing, American Red Cross, Social Work, Nutrition, R&W Association, Spiritual Ministry, CC Volunteer Office, and Executive Office, worked together to bring the most meaningful holiday experience to our patients. Specifically, 34 trees were purchased by R&W for use throughout patient areas, 100 special gifts were purchased for emotionally and/or financially deprived patients, and approximately 118 token gifts were distributed on Christmas morning. As usual, numerous holiday parties were held throughout the Clinical Center. One of the most successful was on Unit 10E. (See page 5, item b)

New this year was the first Holiday Card Decorating Contest. This was held for the purpose of giving Clinical Center volunteers a card made and designed by patients, in appreciation of the volunteers' work at the Clinical Center over the past year. Approximately 27 cards were submitted for consideration; the winning card came from a 3E patient.

The NIH Fire Chief found most of our Christmas trees to be extremely dry and potential fire hazards. He ordered all trees down by December 26, and recommended the use of artificial trees for the future. A Montgomery County fire law informs us that we have no choice. This year, the patients' spirits and morale were greatly affected by having Christmas come and go so fast.

g. Student Fieldwork/Internship Program
We continued to be very involved in training students from various colleges and universities to help them meet their "final" undergraduate and graduate fieldwork requirements in Therapeutic Recreation. This year, we had two seniors each semester, including summer, from University of Maryland, College Park, Maryland, East Carolina University, Greenville, N.C., Longwood College, Farmville, Virginia, and Hood College, Frederick, Maryland.

h. Activity Schedule Improvements
We continued our efforts to improve the appearance and appeal of our weekly schedule of patient recreational events. The three main changes, each of which expedite schedule preparation and add to its "professional" appearance were:

1) the design and weekly use of special blocks highlighting the Patients' Chapel, and this Department (see Attachment #4)

2) utilization of inexpensive, plastic letter guides

3) utilization of rubber stamps for frequently used "headings"

We have been fortunate to have a "full-time" Clinical Center volunteer, trained by this Department, to prepare this schedule. His participation is responsible for facilitating these improvements.

## IV. PROFESSIONAL INVOLVEMENT OUTSIDE OF CLINICAL CENTER

### A. Professional Organizations

Maryland Recreation & Parks Association (Therapeutic Branch)
Cynthia Kauff - Elected Secretary
Holly Anderson - Elected Member-at-Large
Arnold Sperling - Co-Chairperson, Membership Committee

Parkinsonian Society of Greater Washington
Advisory Board Member - Cynthia White, May 1980

### B. Professional Registration (National Therapeutic Recreation Society, N.R.P.A.)

Jane Millman: Recreation Technician II (February 1980)
Eddie Jackson: Recreation Technician II (October 1979)
Cynthia White: Professional Recreation Specialist (provisional) (February 1980)

Joanie Hussey: Therapeutic Recreation Technician II (October 1979)
Janis Partin: Therapeutic Recreation Leader (October 1979)

C. Conferences/Meetings/Workshops

"Role of Recreation Therapy in the Hospital Setting," Uniformed Services University for the Health Sciences (USUHS), Bethesda Naval Hospital, Bethesda, Maryland (class presentation to hospital administrators by Cynthia Kauff), October 1979.

Montgomery College Recreation Curriculum Advisory Board Meeting, Rockville, Maryland (Arnold Sperling), October 1979.

"Therapeutic Recreation in a Hospital Setting," Prince Georges Community College, Largo, Maryland (class presentation to Nursing Home Activity Directors by Arnold Sperling), October 1979.

Annual National Recreation & Park Association Congress, New Orleans, Louisiana (Cindy White/Cynthia Kauff), October 1979.

"Therapeutic Recreation in the Institutional Setting," Hood College, Frederick, Maryland (class presentation to recreation majors by Arnold Sperling), October 1979.

"When A Child Is Dying," Children's Hospital, Columbus, Ohio (two day conference attended by Joanie Hussey and Janis Partin), October 1979.

"Administrative Concerns in Therapeutic Recreation," TR Branch Workshop, MRPA, Rockville, Maryland, (Arnold Sperling/Otis Crutchfield/Holly Anderson/Sue O'Connell/ Cynthia Kauff), November 1979.

"Working With the Dying Child and His Family," Child Life Coordinating Committee, ACCH, Children's Hospital, Washington D.C. (Sue O'Connell/ Holly Anderson/Arnold Sperling/Charles Butler/Joanie Hussey), November 1979.

"Therapeutic Recreation," (class presentation by Ron Hunt to recreation majors), Montgomery College, Rockville, Maryland, December 1979.

Mid-Eastern Symposium on Therapeutic Recreation, Program Committee Meeting (Arnold Sperling), December 1979.

"Role of Therapeutic Recreation," In-Service presented at the Multi-Disciplinary Staff Meeting, Pediatric Oncology Branch, NCI (Joanie Hussey/Holly Anderson/Sue O'Connell/Janis Partin), December 1979.

Mid-Atlantic Forum on Innovative Programming, National Recreation & Park Association, Wilmington, Delaware (Leslie Friel), February 1980.

Therapeutic Recreation Management School, Ogelbay Park, Wheeling, W.Va., March 1980 (Arnold Sperling received his certificate of completion for the two year course; Cynthia Kauff and Otis Crutchfield successfully completed their first year), March 1980.

"Observing and Recording Behavior of the Hospitalized Child," ACCH Affiliate Seminar, Holy Cross Hospital, Silver Spring, Md., March 1980 (Holly Anderson/Janis Partin/Vera Sales/Charles Butler), March 1980.

"Research on Children in Health Care Settings," ACCH Affiliate Meeting, (Janis Partin), March 1980.

"Integrating the Creative Arts into Recreation Programs for Special Populations," MNCPPC, Montpelier Cultural Center, Laurel, Maryland (Arnold Sperling/Holly Anderson/Patty Shomper), April 1980.

"Seminar on Death and Dying," CC Education and Training Section, NIH, Bethesda, Maryland (Charles Butler/Janet Amass/Arnold Sperling/Holly Anderson), April 1980.

"Seminar on Death and Dying," CC Education and Training Section, NIH, Bethesda, Maryland (Joanie Hussey - Panelist and Instructor), April 1980.

Recreation Leadership Community Advisory Committee Meeting, Montgomery College, Rockville, Maryland (Arnold Sperling), April 1980.

Annual Conference on Parks and Leisure Services. Ocean City, Md. (Cindy White/Arnold Sperling/Holly Anderson), April 1980.

a. "The What, Who and Why of Therapeutic Recreation," (Arnold Sperling, Panelist)
b. "Innovating Programming in Therapeutic Recreation," (Cindy White, Panelist)

Mid-Eastern Symposium on Therapeutic Recreation, National 4H Center, Washington D.C., (Arnold Sperling/Patti Tepsic/Cindy White/Cynthia Kauff/Leslie Friel/Jane Millman/Otis Crutchfield/Charles Butler), May 1980.

a. "The Outdoor Continuum," (Charles Butler, Panelist).
b. Arnold Sperling served on the Program Committee for this Symposium and chaired four educational sessions.

Seminar on Adolescent and Childcare Behavior, Psychiatric Institute, Washington D.C. (Patti Tepsic), June 1980.

"Interdisciplinary Approach: Fact or Fantasy?," National Conference of the Association for the Care of Children in Hospitals, Dallas, Texas (Janis Partin), July 1980. (See page 6 for details).

## V. FUTURE OBJECTIVES

1. continued emphasis in working with "special" patients on a one-to-one basis
2. greater communication, both verbal and written, with other hospital disciplines and among our own staff
3. continued development of a standard means of patient documentation and evaluation
4. charting/documentation of patient behavior into the Clinical Center Medical Information System
5. more involvement in the leisure counseling aspects of therapeutic recreation

Therapeutic Recreation Section

ATTACHMENT #1

## 1. Adult Recreation Referral Program

| | Number of Referrals | Number of Responses |
|---|---|---|
| NIAID | 714 | 655 |
| NIAMDD | 471 | 421 |
| NICHD | 62 | 59 |
| NCI | 324 | 273 |
| NEI | 42 | 28 |
| NHLBI | 232 | 165 |
| NINCDS | 178 | 143 |
| NIMH | 222 | 165 |
| SACP | 169 | 169 |
| | 2414 | 2078 |

## 2. Children's Play Program

| | Patients | Child Visitors | Total |
|---|---|---|---|
| NIAID | 73 | 23 | 96 |
| NIAMDD | 55 | 23 | 78 |
| NICHD | 272 | 67 | 339 |
| NCI | 126 | 65 | 191 |
| NEI | 7 | 9 | 16 |
| NHLBI | 50 | 26 | 76 |
| NINCDS | 59 | 22 | 81 |
| NIMH | 70 | 35 | 105 |
| SACP | 90 | 67 | 157 |
| | 802 | 337 | 1139 |

## 3. National Institutes of Mental Health

| | |
|---|---|
| Unit 3 East | 287 patients |
| Unit 3 West | 126 patients |
| Unit 4 East | 131 patients |
| Unit 4 West | 84 patients |
| Unit 6D | 72 patients |
| | 700 |

## 4. National Cancer Institute - Special Unit Program

| | |
|---|---|
| Unit 10 East | 740 patients involved |
| Unit 12 East | 561 patients involved |
| Unit 12 West | 429 patients involved |
| Unit 13 East | 578 patients involved |
| | 2308 |

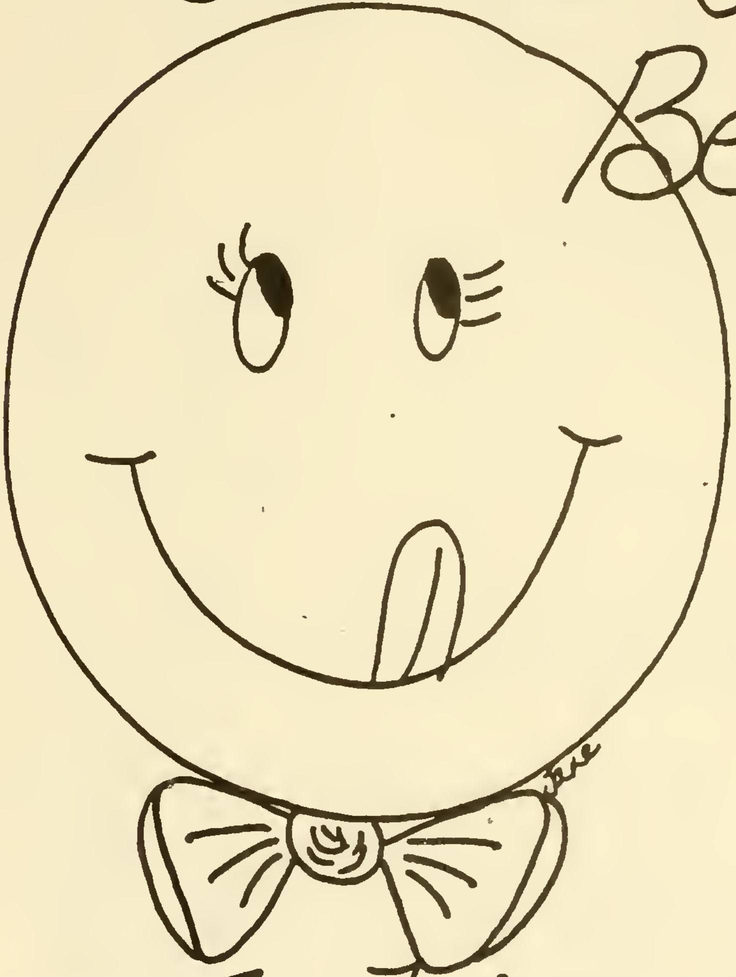
## Patient Library Section

ATTACHMENT #2

### Reading Utilization

| Item | Number on Hand | Number Circulated |
|---|---|---|
| Stereo Record Players | 31 | 285 |
| Records | 730 | 3824 |
| Talking Book Machines | 5 | 25 |
| Talking Books | 39 | 77 |
| Magnifying Glasses & Bed Specs | 9 | 11 |
| Bookracks | 3 | 15 |
| Earphones | 7 | 53 |
| Cassette Players | 6 | 114 |
| Cassettes | 40 | 106 |

# Newcomer's Easy Guide To Bethesda



## Where To Find It all !

A patient handbook of fun, food & facts

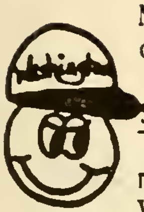
# Welcome ...

There is lots to do and see in the Bethesda area. This guide will help you find activities to enjoy during your stay in the area.

## Calendars of Events

Weekly calendars of events are available in both Washington daily papers. The "Weekend" section of the Washington Post appears on Fridays and the "Calendar" section of the Washington Star appears on Sundays.

A monthly clendar of events appears in the "Washingtonian Magazine" , which can be purchased at the concession shop on the B1 level of the Clinical Center.



## Sightseeing

For those interested in sightseeing, the DC area has much to offer. A good starting point would be the National Visitor Center (Union Station) where you will find maps, info, restaurants, a bookstore, and metrobus, tourmobile, and metro stops.

Some sights you may not want to miss include:

The White House
1600 Pennsylvania Ave., NW
456-2200

Washington Monument
15th St. near Constitution Ave. SW
426-6700

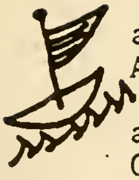
The U.S. Capitol
east end of the Mall on Capitol Hill
225-6827

John F. Kennedy Center for the Performing Arts
2700 F St., NW
254-3600

National Zoological Park
3000 block of Connecticut Ave.,NW
387-7400

The Smithsonian Institution
most buildings are located on the mall
for general info - 381-6264
Recorded announcements of events - 737-8811

At certain times throughout the year, the Patient Activities Department offers sightseeing trips to DC attractions. Information on these trips is available through the Patient Activities Department (496-2276).



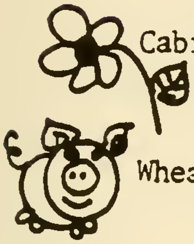
Also close to Bethesda are many nearby towns which offer attractions of their own including:

Annapolis, Md. -
the state capital of Maryland with its waterfront and historic areas (ie. state house, U.S. Naval Academy)

Georgetown, Wash., DC -
located on the Potomac River with such attractions as the C&O Canal , Dumbarton Oaks Gardens, and its unique shopping district

Olde Towne, Alexandria, Va. -
another river town similar to Georgetown with quaint shops, taverns, etc.

## Parks



The area surrounding NIH has many parks including the following:

Cabin John Regional Park - 7400 Lux Court, Rockville (299-4555)
attractions include a playground, miniature train ride, a small farm animal zoo, picnic area, baseball diamonds, handball and tennis courts, and an ice rink

Wheaton Regional Park - Wheaton, Maryland (622-0056)
includes Old MacDonald's Farm, children's playground, train ride, bike and hike trails, pony rides, ball fields, ice rink, lake

Great Falls, Maryland - 11710 MacArthur Blvd., Potomac,Md. (299-561
Canal Museum, snackbar - impressive natural falls where Potomac Ri
drops more than 70 feet over numerous falls and rapids

or....if you enjoy gardens, why not try a visit to

Brookside Gardens - 1500 Glenallen Ave., Wheaton, Md. (949-8230)
a 50-acre public garden and greenhouse - Christmas, Easter, and autumn displays are annual features

For recorded info on National Capital Parks (parks within DC) events, call 426-6975.

## For Sports Fans

Baseball - Sorry, Washington has no professional baseball team. The Baltimore Oriole's is the closest professional team for DC baseball buffs.

Basketball - Washington's pro team, the Bullets, play at the Capital Centre in Landover, Maryland (350-3900) from October thru early April. The University of Maryland Terrapins can be seen at the University's Cole Field House in College Park (454-2121).

Football - The Washington Redskins play at Robert F. Kennedy Stadium from early October to mid-December, but seats are nearly impossible to obtain (546-2222). For a look at college football, the University of Maryland Terrapins play home games at Byrd Stadium in College Park.

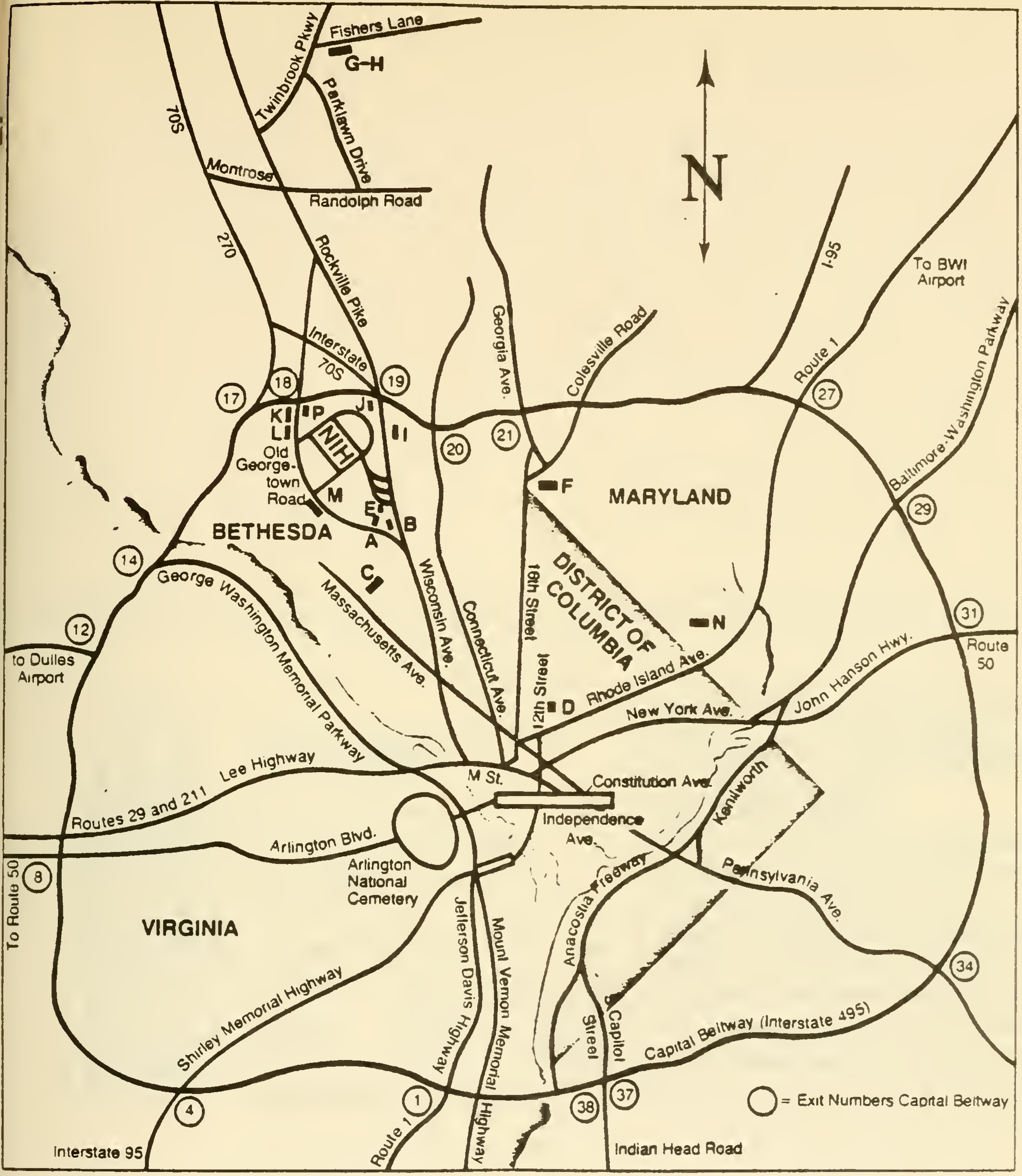
Magic Pan Creperie
Montgomery Mall, Rockville 365-0500
crepes of all kinds
moderate - expensive
Emerson's
Wildwood Shopping Center, Bethesda 530-5300
steak and salad
moderate
Tastee Diner
7731 Woodmont Ave., Bethesda 652-3970
open 24 hours
inexpensive
For fast food - travel down Rockville Pike toward Rockville to find Roy Rogers, Ginos, Arbys, and Shakey's Pizza Parlor.

And if you have a craving for dessert, some popular area ice cream parlors include
Gifford's Ice Cream
7623 Wisconsin Ave., Bethesda 652-1664
Swenson's Ice Cream Parlor
Bethesda Square Shopping Center, 7710 Woodmont Ave, Bethesda 986-8744
or Montgomery Mall, Rockville
and Tiffany's Bakery at White Flint Mall has delicious, although expensive, goodies.

## Shopping

Shopping in the Bethesda area includes...
White Flint Mall
11301 Rockville Pike, Rockville
very expensive for shopping, but a nice place to visit
Montgomery Mall
Democracy Blvd., Bethesda
3 large department stores and many small shops
Wildwood Shopping Center
Old Georgetowne Rd., Bethesda
grocery store, drug store and small shops
Georgetowne Square Shopping Center
10400 Old Georgetowne Rd., Bethesda
movie theatres, restaurant, craft shop and other small shops

We hope this guide has been of help to you. If you have any questions, feel free to contact the Patient Activities Department at 496-2276.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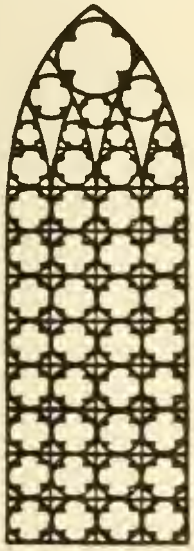

## Chapel

On the 14th floor.

Chapel is open at all times.

All Services are broadcast over NIH radio.

Regular services are held as follows:

| | | |
|---|---|---|
| **Catholic:** | **Sunday** | **11:15 a.m.** |
| | **Daily** | **11:15 a.m.** |
| **Jewish:** | **Friday** | **4:30 p.m.** |
| **Protestant:** | **Sunday** | **10:00 a.m.** |

**Chaplain Telephone 496-3407**

## Patient Activities Schedule

Published weekly by the Patient Activities Department, The Clinical Center, N.I.H., Bethesda, Maryland 20205 for all Center Patients, Volunteers, and Staff.

**For Information, Call 496-2276**

October 1, 1979 through September 30, 1980

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

PHARMACY DEPARTMENT

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October 1, 1979 through September 30, 1980

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

PHARMACY DEPARTMENT

## I. MISSION AND GOALS

The mission of the Pharmacy Department is to provide comprehensive, properly coordinated, pharmaceutical services of the highest quality to patients and staff of the Clinical Center in support of biomedical research. To accomplish this mission, the goals are as follows:

1. To have pharmaceutical services support which facilitates clinical pharmacy practice;

2. To have accountable, documented clinical pharmacy practice;

3. To have pharmacy education programs which augment clinical pharmacy practices;

4. To have a pharmacy research program which improves patient care; and

5. To occupy a locally, nationally, and internationally recognized position in pharmacy.

The Pharmacy Department consists of the Pharmacy Service, Pharmaceutical Development Service, and the Office of the Chief.

The Pharmacy Service interprets and transcribes medication orders, dispenses and monitors drugs through the use of patient drug profiles, and dispenses all medications ordered for patients in the Clinical Center. This Service fulfills these responsibilities by dispensing 725,000 unit doses yearly (individually packaged and labeled dispensing doses) to each patient; it fills drug orders for outpatients, discharged patients, and patients who are on pass. This Service prepares all intravenous additive solutions (over 150,000 bottles yearly) ordered for inpatients and outpatients; it fills drug requisitions for clinics and other patient care areas not on the unit dose system; it compounds and packages products not available commercially and maintains all investigational drug dispensing records. The Pharmacy Service also provides drug information and clinical services for physicians, nurses, and patients.

Pharmaceutical Development Service (PDS) is responsible for the registration, inventory control, development, formulation, and manufacturing of investigational drugs used for patients in the Clinical Center. When the drug is available in the desired dosage form, PDS is responsible for procurement, control, and registration of these drugs and acts as a custodian for these

drugs. If the drug is not available in the dosage form needed for a particular research protocol, PDS formulates and manufactures the dosage forms and supplies the physicians with necessary analytical, manufacturing, quality control, and developmental data for submission to FDA in support of Investigational New Drugs (IND). The analytical laboratory of PDS provides the necessary quality control for drugs manufactured in PDS and also conducts compatibility and stability studies of various drug combinations used in Clinical Center patient care. PDS has also recently established a clinical pharmacokinetic research laboratory to collaborate with the physicians in clinical pharmacokinetic studies of various drug protocols and to provide, where feasible, research-oriented analytical support for determination of drugs and their metabolites in the biological fluids of patients.

The Office of the Chief provides overall policy and direction to the Services and centralized procurement of approximately $2,500,000 worth of drugs and supplies.

## II. DEPARTMENT ACTIVITIES

On October 15, 1979, the Central Sterile Supply Service of the Pharmacy Department, with a staff of 35 people, was administratively reorganized under the Materiel Handling Department. The Service had been operated by the Pharmacy Department since the opening of the Clinical Center.

As seen in Table I, the number of total outpatient prescriptions filled for patients on pass, discharged or in the clinics increased from 80,746 to 85,063 (5%). Intravenous admixtures increased from 149,434 to 162,676 (10%); sterile compounded items, such as prefilled syringes and vials increased from 3,961 to 5,386 (36%), and drug vials reconstituted increased from 31,739 to 41,688 (31%). The large increases seen in sterile compounded items and reconstituted vials were due to the extra workload generated by the Intravenous Additive Unit (IVAU) satellite in the clinic and by the number of chemotherapy drugs with stability less than 24 hours, prepared by the IVAU.

The unit doses dispensed increased slightly from 692,568 to 695,886 (0.5%). Items bulk-compounded decreased from 558,600 to 440,757 (21%). This was due to increased availability of commercially packaged unit dose items and an improved system of stock control through unit dose dispensing. The composite category "other items" showed a substantial increase from 201,782 to 246,406 (22%). Contributing to this increase were: a 36% increase in "issues to IVAU" due to the IVAU satellite; an increase in floor stock requisition items, partly because 1980 was the first full year of operation of the Medical Intensive Care Unit; and an increase in narcotic requisitions dispensed.

The number of requests for service (from 11:00 PM - 7:30 AM) by the pharmacy officer of the day increased substantially from 9,506 to 13,629 (43%). This may be due to increased awareness of Clinical Center personnel to Pharmacy's 24-hour service.

As can be seen in Table I, the total number of units formulated, developed, and issued by PDS increased from 937,858 to 1,390,008 (48%); the number of requests for service increased from 1,152 to 1,428 (24%); and new investi-

gational drugs processed increased from 114 to 128 (13%). The large increase in the number of units formulated, developed and issued was due to a significant increase in requests for services (24%) and in the number of double blind studies involving the use of very large amounts of drugs such as: bromocryptine, lisuride, verapamil, and propranolol.

Because of renovation of the 2-West nursing unit, the entire operation of the Department was disrupted while temporary partitions were installed. This required the relocation of the outpatient pharmacy operation from the main pharmacy to Room 1S-263. Other pharmacy operations and areas such as unit dose, IV admixtures bulk compounding, procurement and drug storage were forced to operate in severely reduced space which caused many problems. However, there were advantages associated with the new location: relief of some of the overcrowding in the main pharmacy; a larger and therefore a safer work area for the outpatient pharmacy. It is expected that the outpatient pharmacy will remain in Room 1S-263 until finally relocated to serve the ACRF.

Pharmacy submitted approximately 125 MIS computer change requests to the Office of Clinical and Management Systems.

## III. MAJOR PROGRESS IN SERVICES, TRAINING, DEVELOPMENT, AND RESEARCH SERVICES

### Service

The Pharmacy Department Formulary was totally revised, updated, and distributed to the medical staff and patient care areas in the Clinical Center. The Formulary contains not only drugs routinely stocked but also extensive information on pharmacy operations and services available and some tables of useful drug information.

In November 1979, at the request of the Director of the Clinical Center, three distinguished leaders in the field of hospital pharmacy from around the country site-visited the Department for 2 days to evaluate the operations of the Department and make recommendations for improvement. The site team was headed by David Zilz, Director of Pharmacy, Central Respiratory and Materiel Services, University of Wisconsin, Madison and current president of the American Society of Hospital Pharmacists. The other members of the team were William Smith, Director of Pharmacy and Central Services, Memorial Hospital Medical Center, Long Beach, California, and Paul Pierpaoli, Director of the Department of Pharmacy Services, Medical College of Virginia, Richmond. The site visit team submitted a 5-page report to the Director of the Clinical Center. Each Service Chief in the Department commented on the report and several of the recommendations were implemented. The administrative, senior staff of the Department felt that this was a most constructive, worthwhile and beneficial experience.

One of the recommendations made by the site visit team was to initiate more pharmacist clinical services. Comprehensive clinical pharmacy programs were initiated with the Pediatric Oncology Branch, NCI, and on 5-East and 5-West, NINCDS. The 5-East and 5-West nursing units were selected as Phase I of a discharge counseling program for the Clinical Center which included criteria

for patient assessment and selection as an approach to counseling and the use of recommended methods of documentation.

Other recommendations were implemented such as: moving the outpatient pharmacy to the larger area in the Department, and making it less crowded and a safer working environment for the volume of prescriptions dispensed; site visiting other hospitals having large ambulatory care programs and attending an Institute on Ambulatory Care Pharmacy Services; reorganizing the IV and UD dispensing units for more efficient and effective operation; and expanding the clinical pharmacokinetics research program.

A time and motion study on work activity in the IVAU led to a change from a 12-hour mixing and delivery schedule to a 24-hour system. The workload is now divided into 3 groups (by nursing units) throughout the day. Orders are prepared at optimal times with better input from the nursing units, via pharmacy followup, regarding the IV solution changes.

A 6 month review of the IVAU satellite in the clinic was written and distributed to NCI. The service is considered extremely valuable both by physicians and nurses. Intravenous admixture solutions are being prepared in a biological safety cabinet, as opposed to the open air, nursing and physician time is being saved, and patient drug profiles for protocol drugs are being maintained and monitored by pharmacists.

The IVAU established a system for the uniform preparation of certain cardiac drugs (e.g., dopamine, lidocaine) for the Anesthesiology Department, expanded the regular preparation of plasmapheresis solutions to include NIMH, NINCDS, and NIAMDD programs, and initiated the preparation of certain short stability chemotherapy drugs (e.g., mechlorethamine, ICRF-187) for patients in the Medicine Branch, NCI.

Comprehensive clinical pharmacy programs were initiated with the Pediatric Oncology Branch (POB), NCI, and on 5-East and 5-West, NINCDS. For NCI, it included development of a graphic chemotherapy profile, for both inpatients and outpatients, medication counseling for discharged patients, monitoring high dose methotrexate, and inservice education for POB nurses on IV push techniques and drug compatibility. For NINCDS, it included taking drug histories on selected patients, monitoring patients on glucocorticoid therapy, and a drug counseling program for discharged patients which, we hope, will serve as a prototype for future drug counseling in the Clinical Center.

A discharge counseling program for the Clinical Center was written which included patient assessment and selection criteria, patient counseling, and methods of documentation. The 5-West and 5-East nursing units were selected as the pilot units. The program was reviewed and approved by the Pharmacy and Therapeutics Subcommittee.

A more convenient and practical drug box was procured for use in cardiopulmonary resuscitation. The box was reviewed and approved by the CPR Committee and implemented throughout the hospital.

Pharmacy personnel assisted the Outpatient Department in organizing a system of stock ordering and control in the clinics. This was necessary because of the Outpatient Department reorganization which changed nursing support and function.

The Pharmacy Bulletin, the Pharmacy Department's professional newsletter distributed to the medical and nursing staff, was totally revamped this year. The format was changed and the scope of information provided was expanded.

One of the major achievements of PDS over the last year has been the expansion of its pharmacokinetic research and services in addition to the regular responsibilities of formulation, registration, and quality control of investigational drugs. In the past year, PDS has made significant progress in the area of pharmacokinetics of drugs. PDS continued to provide analytical services for methotrexate and carbamazepine blood and CSF levels. In addition, PDS started collaborative research on carbamazepine pharmacokinetics, intrathecal Ara-C pharmacokenetics, distribution and kinetics of thiopental in hyperthermia patients, and general behaviour of drug distribution in rabbit eye tissue after both systemic and intraocular administration.

PDS revised procedures for investigational drug inventory which made for overall smoother operations. The analytical unit carried out regular quality control work, and in addition to continuing various long term drug stability research projects, has worked on various practical projects of immediate use in the Pharmacy Department, e.g., absorption of nitroglycerin in IV tubing, checking of various wrapping materials for light permeability, and assorted drug identity problems. In the formulation unit, PDS applied for patents on an ethiodol emulsion formulation and 5-azacytidine sodium bisufite pro-drug.

As of June 1980, PDS enters drug blood/CSF level assay results it performs into the Clinical Center MIS system. Currently, this includes the methotrexate levels for POB patients. These results are retrieved in a manner similar clinical pathology test results.

## Training

A number of formal inservice training programs for the Nursing Department were conducted by the Pharmacy Department including: "Intravenous Push Technique and Related Drug Information", "Orientation to Pharmacist's Role in Discharge Counseling," "Use of Dexamethasone;" "Use of Mannitol," "Use of Anthracendione," "Cardiac Emergency Drugs," "Use of Drug Information Sources on the Nursing Unit," and "Dialysis and Drug Therapy."

The film "Medications and You" was obtained and edited, and arrangements were made with the Clinical Center Office of Clinical Reports and Inquiries to show the film daily on the Clinical Center television network to patients being discharged.

The Pharmacy Department's internal staff development program was further organized and expanded in scope. Formal instruction in the research of drug information and monitoring of drug interactions was presented to all staff members. In addition, clinical update programs were presented to staff that

covered such topics as: "Drugs and Hemodialysis," "Therapeutic Review of Bretylium, Propranolol, Dantrium, and Insulin," "Guidelines on Patient Monitoring," "Febrile Seizures in Children," "Use of Streptokinase," and a variety of unique and interesting case reports.

An internal newsletter, "Drug Information Notes," was established which contains abstracts of the current medical and pharmaceutical literature which are of interest and importance to the Pharmacy staff.

Five pharmacy residents completed the one year Pharmacy Department's hospital residency program which is accredited by the American Society of Hospital Pharmacists. The experience and the logistics of handling five residents was invaluable, and a number of program changes were made for the coming year. The philosophy and objectives of a hospital residency at the Clinical Center will emphasize staff responsibilities and administrative functions. A residency program is planned that will include an eight-week rotation in each of five different areas of the Clinical Center pharmacy.

Two undergraduates from the University of Maryland School of Pharmacy were trained in a structured externship program (Professional Experience Program) for two consecutive months. The program is designed to give the students practical experience in hospital pharmacy. One fifth year undergraduate student in Howard University College of Pharmacy's Government Work-Study Program spent 900 hours training in PDS. One pharmacy graduate student from the University of Southern California Pharmacy Department Program spent three months training in PDS as part of the Public Health Service Commissioned Officer Student Training and Externship Program (COSTEP) and his residency requirement towards his Pharm. D. degree. One undergraduate pre-pharmacy student from Purdue University in a Work-Study Program spent 450 hours training in PDS.

Two fifth year undergraduates from Philadelphia College of Pharmacy and Science and Purdue University's College of Pharmacy spent 3 months training in the outpatient pharmacy and the unit dose dispensing unit, as part of the PHS's COSTEP program.

Development

The Unit Dose Dispensing Unit's processing operations were totally reorganized to improve efficiency and effectiveness. This involved the restructure of workday assignments, change in cart delivery times, and implementation of workload monitoring checkpoints throughout the day. As a result of this more efficient use of both professional and technician staff, we were able to expand staff level clinical functions and responsibilities.

A new position of Pharmacy Coordinator for Computer Projects was developed for the Department. The coordinator, under the direction of the Chief, Pharmacy Department, is responsible for the research, planning, development, implementation, coordination, and evaluation of all pharmacy-related computer projects. The coordinator also acts as liaison between the Pharmacy and the Office of Clinical and Management Systems, Clinical Center Management, Technicon Company, the Division of Computer Research and Technology, and MIS.

The position of controlled drug distribution technician was developed and implemented. This position was formerly held by a pharmacist. The new position resulted in more effective utilization of technical personnel and improved service and delivery of controlled drug distribution to patient care areas.

The hospital pharmacy's residency program was restructured to provide more flexibility and to emphasize the clinical and administrative aspects of the residents' training. The staff service responsibilities of the residents were increased in order to enlarge their practical experience and to more effectively utilize staff level pharmacists.

The Department's 5 pharmacy residents were each assigned an individual project for the year. The projects were service-related and included: time and motion study of unit dose processing operations--a good deal of the information compiled in this study was useful in the reorganization of the unit dose processing operation; compilation of a data base of drug-drug, drug-lab test, and drug-disease state interactions--much of this data was used in an instuctional program presented to the staff; compilation of intravenous drug data sheets--these sheets provide comprehensive information on commerical and investigational parenteral drugs and are used as a primary reference by pharmacists; review and reorganization of bulk compounding procedures and services; and development of a flow-sheet for monitoring of fluids and electrolytes.

The functions required in the development of an automated outpatient drug profile system and a drug inventory control system were identified by the Pharmacy. The outpatient drug profile system will provide for effective monitoring and record keeping of all drugs received by clinic, pass, and discharged patients. In this system a Pharmacy-MIS to mini-computer link is planned for functions not presently available to improve patient care: an input/output feature to control drug stock ordering from suppliers, a specialized management report to list expired stock, to list so as to maintain optimum inventory levels and to forecast drug usage trends.

A Pharmacy MIS information bulletin was initiated and is being circulated to the Pharmacy Department staff. This bulletin contains: recent computer updates and changes, proposed changes, and a facts and features section. A discharge counseling-teaching pathway was developed in the Clinical Center MIS system for pharmacy. This is being used to document medication counseling performed by pharmacists when patients are discharged. A program was developed and is being maintained through the NIH WYLBUR program, to sort and alphabetically list the POB patients on its fever study. This program reduces the time required to process patients from POB in the Outpatient pharmacy. A chart listing the terminology used for the MIS medications order was developed and has been posted by each Visual Matrix Terminal to assist pharmacy users in processing MIS orders and as a training guide for new staff.

## Research

Stability of chlorambucil in aqueous solution was studied using HPLC. The results showed that previously published data by other researchers were

incorrect. Detailed chemical kinetic studies are in progress to obtain practical kinetic data applicable under physiological conditions and to understand the mechanism of nitrogen mustard hydrolysis.

Incompatibility of povidone-iodine combination with Lavacol was studied. It was concluded that acetone and methyl butyl ketone present as denaturents in Lavacol (Parke-Davis Company) consumed the free iodine and may influence the bactericidal effect of Povidone-Iodine.

Clinical studies for diagnosis of liver cancer with ethiodol emulsion previously developed in the PDS laboratory is continuing with a slightly higher dose of emulsion which improved the contrast in the CAT scans of liver after injection of the emulsion. As an adjunct to this project, rats are being injected with monosized polystyrene beads with a fluorescent coating to determine if various tissues absorb the particles differentially.

Pharmacokinetics of thiopental sodium (Pentothal, Abbot Laboratories), in hyperthermia patients are being studied to understand why a much larger dose of the barbiturate is needed to keep the patients sedated.

Serum and CSF carbamazepine levels of patients are being analyzed and evaluated to see if any correlation exists between the clinical response and levels of carbamazapine and/or its major metabolite carbamazepine 10-11 epoxide. Absorption and distribution kinetics of carbamazepine are being studied in patients receiving both acute and chronic dosing of the drug.

Permeability of various drugs into eye tissue is being studied using two ionic and two nonionic drugs after administering the drugs systemically or into the posterior chamber of the rabbit eye. Our results so far have shown (1) that membranes separating the blood and eye chambers and the membrane separating the posterior and anterior chamber of rabbit eye are basically similar to other biological membranes in the body and that (2) they are more permeable to nonpolar and nonionic drugs than to highly water soluble and ionic drugs.

## IV. FUTURE OBJECTIVES

Future departmental objectives are:

1. To increase pharmaceutical service provided in the IVAU Medicine Branch clinic satellite by including patient medication counseling and the dispensing of oral protocol medications;

2. To expand the role of the pharmacist in the area of clinical research support through specific in-depth protocol monitoring for individual clinical investigators;

3. To improve and expand the Pharmacy Service staff development program by providing pharmacists with the necessary training and knowledge to function effectively in Department defined clinical pharmacy programs;

4. To standardize the rates of administration and amounts of infusion diluent (D5W, NS, etc.) for all intravenous antibiotics ordered in the Clinical Center;

5. To initiate a study to determine the feasibility and cost effectiveness of selective unit dose packaging of stable parenterals;

6. To further expand PDS's clinical pharmacokinetic research and services and plan to hire a pharmacokineticist and a chemist for the clinical pharmacokinetic laboratory;

7. To participate in the computerized Phase II Material Management System. The required computer hardware will be located within the Pharmacy Department, and procurement, obligating, and receiving information will be input directly into the computer by Pharmacy personnel;

8. To continue to develop a computerized drug inventory control and outpatient drug profile system;

9. To enclose the Pharmacy drug storeroom with a wire cage and limit access to the area to authorized personnel only;

10. To complete the final internal work flow layout, planning, and selection of equipment and fixtures for the ACRF Pharmacy.

## Table I
## Pharmacy Department Statistical Data

| | 1976 (Fiscal) | 1977 (Fiscal) | 1978 (Fiscal) | 1979 (Fiscal) | Est. 1980 (Fiscal) |
|---|---|---|---|---|---|
| **PHARMACY SERVICE** | | | | | |
| Outpatient prescriptions (for pass, discharged, and clinic patients) | 73,693 | 81,022 | 83,887 | 80,746 | 85,063 |
| IV additives (bottles) | 112,845 | 140,930 | 163,978 | 149,434 | 162,676 |
| Drug vials reconstituted by IV Additive Unit | 43,320 | 42,520 | 41,312 | 31,739 | 41,688 |
| Sterile compounded items | 5,247 | 6,453 | 5,711 | 3,961 | 5,386 |
| Unit doses dispensed | 254,103 | 561,273 | 594,753 | 692,568 | 695,886 |
| Prepackaged items | 365,723 | 638,862 | 573,207 | 558,600 | 440,757 |
| Other items (mail-outs, bulk-compounding items, narcotics, requisitions, issues to IV area) | 282,727 | 298,061 | 258,335 | 201,782 | 246,406 |
| **PHARMACEUTICAL DEVELOPMENT SERVICE** | | | | | |
| Units developed and issued | 567,911 | 870,647 | 750,740 | 937,858 | 1,390,008 |
| Requests processed | 869 | 1,043 | 1,132 | 1,152 | 1,428 |
| Investigational drugs registered | 527 | 596 | 613 | 772 | 768 |
| New investigational drugs processed | 92 | 136 | 125 | 114 | 128 |
| **PHARMACY OFFICER OF THE DAY** | | | | | |
| Number of requests for service | 13,254 | 17,376 | 13,523 | 9,506 | 13,629 |
| **MAIL-OUT PRESCRIPTIONS** | | | | | |
| Number of prescription packages mailed | 1,527 | 1,558 | 2,048 | 2,385 | 2,264 |

## Professional Activities

Dr. Gallelli, Chief of the Department, was elected to the United States Pharmacopeial Committee of Revision, 1980-1985. The Revision Committees cover both standards-setting activities and the provision of patient drug information in 32 categories. The Division Executive Committee comprises the Chairmen of 15 subcommittees of which Dr. Gallelli is Chairman, Parenteral Products. USP Revision Committee members are elected for 5-year terms. Their service is entirely voluntary, but their decisions lead to revisions in the United States Pharmacopeia and the National Formulary and are enforceable under state and federal laws and regulations.

PUBLICATIONS

Chatterji, D.C.: "Potential Errors in Kinetic Studies of Chlorambucil Hydrolysis based only on Chloride Ion Determination", In Press, J. Pharm. Sci., 1980.

Chatterji, D.C., and Hood, J.C.: "Incompatibility of Betadine with Lávacol". Am. J. Hosp. Pharmacy, April 1980.

Vermess, M.D., Doppman, J.L., Fischer, R.I., Sugerbaker, P., Chatterji, D.C., Luetzeler, J., Grimes, G., Girton, M. and Adamson, R.N.,: "Clinical Trials with a Newly Developed Intravenous Liposoluble Contrast Material for Computed Tomographic Examination of Liver and Spleen", In Press, Radiology, 1980.

| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do **NOT** use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CI 05010-01 PHAR |
|---|---|---|

PERIOD COVERED

October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

Potential Errors in Stability Studies of Chlorambucil using Chloride ion production data.

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Dulal C. Chatterji, Acting Assistant Chief

COOPERATING UNITS (if any)

LAB/BRANCH

Pharmaceutical Development Service, Pharmacy Department

SECTION

INSTITUTE AND LOCATION

CC, NIH, Bethesda

| TOTAL MANYEARS: | PROFESSIONAL:<br>0.2 | OTHER:<br>0.1 |
|---|---|---|

CHECK APPROPRIATE BOX(ES)

☐ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☒ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

It was shown using a stability specific HPLC analysis of chlorambucil that literature reports of rates of hydrolysis using chloride ion liberation data overestimated the stability of chlorambucil in aqueous solutions.

PHS-6040
(Rev. 10-76)

Serial No. Z01 Cl 05010-01 PHAR
Pharmacy Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 - September 30, 1980

Project Title: Potential Errors in Stability Studies of Chlorambucil using Chloride Ion Production Data.

Previous Project Number: None

Principle Investigator: Dulal C. Chatterji, Ph.D.

Other: None

Cooperating Units: None

Man Years:
Total: 0.3
Professional: 0.2
Other: 0.1

## Project Description

### Objective:

To study the hydrolysis kinetics of chlorambucil.

### Method Employed:

HPLC was used to analyze chlorambucil in presence of its degradation products.

This was used to follow the rate of hydrolysis of chlorambucil. The rates were also obtained by measuring the rate of chloride ion liberation using a chloride ion titrator.

### Significance in Biomedical Research:

It was found out that the earlier literature data on the stability of chlorambucil in particular and nitrogen mustards, in general, which were obtained by following the rate of chloride ion liberation was inaccurate. The actual hydrolysis rate was 2-3 fold faster, and this finding has significance in the bioavailability and disposition of various dosage forms of nitrogen mustards.

### Proposed Course:

Extend the kinetic work on Chlorambucil to cover the entire physiological range, clarify the mechanism of nitrogen mustard hydrolysis and its consequences on the biodisposition of nitrogen mustards.

## Honors and Awards:

None

## Publications:

Chatterji, D.C., "Potential Errors in the Kinetics of Chlorambucil Hydrolysis using Chloride Ion Determination," In Press, J. Pharm. Sci. 1980.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE
PROJECT NUMBER (Do NOT use this space)

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NOTICE OF
INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CL 05011-01 PHAR

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

Clinical Pharmacokinetics of Carbamazepine

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Robert Post, M.D., NIMH

Dulal C. Chatterji, Ph.D., Pharmacy Dept.

Raymond F. Greene, M.S., Pharmacy Dept.

Thomas Udhe, M.D., NIMH

COOPERATING UNITS (if any)

NIMH

LAB/BRANCH
Pharmaceutical Development Service

SECTION

INSTITUTE AND LOCATION
CC, NIH, Bethesda

| | | |
|---|---|---|
| TOTAL MANYEARS:<br>0.5 | PROFESSIONAL:<br>0.3 | OTHER:<br>0.2 |

CHECK APPROPRIATE BOX(ES)

x (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Tegretol (CBZ) pharmacokinetics was determined in patients undergoing treatment for mania and depression. A HPLC method was developed to analyze CBZ and its epoxy metabolite in plasma and CSF. Levels of CBZ for routine clinical use was determined by EMIT. It was found that although the levels of CBZ or its epoxide in plasma has no correlation with the efficacy of CBZ among various patients, in the patients that do respond, CBZ plasma levels gave good correlation with the clinical improvement of the patient.

Serial No. Z01 Cl 05011-01 PHAR
Pharmacy Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 - September 30, 1980

Project Title: Clinical Pharmacokinetics of Carbamazepine.

Previous Project Number: None

Principal Investigators: Robert Post, M.D., NIMH
Dulal C. Chatterji, Ph.D., Pharmacy Dept.

Other: Raymond F. Greene, M.S., Pharmacy Department
Thomas Udhe, M.D., NIMH

Cooperating Unit: NIMH

Man Years: Total: 0.5
Professional: 0.3
Other: 0.2

## Project Description

### Objective:

To study the pharmacokinetics and monitoring of the steady state levels of carbamazepine (CBZ) in patients undergoing treatment for mania and depression.

### Methods Employed:

The blood samples were drawn from patients both during the loading phase and steady state phase with CBZ. CSF samples were drawn only from patients in steady state. Protocol for blood sampling during the acute and chronic dosing phase were designed for studying both absorption and elimination kinetics. The samples were analyzed for CBZ and its major metabolite, 10-11 epoxide by HPLC.

### Major Findings:

The HPLC methodology developed was very useful for fast and precise determination of CBZ and its metabolite in plasma and CSF. It appeared that, in general, the plasma levels of either the drug or the epoxide does not correlate with the therapeutic efficiency of CBZ. However, in a patient that does respond, CBZ levels in plasma correlates well with the clinical improvements in the patient.

## Significance in Biomedical Research:

The study would contribute to the knowledge of mechanism of action of CBZ and would help in designing dosage regimen for the administration of CBZ during chronic dosing.

## Proposed Course:

Accumulate data on more patients as to the relationship of CBZ dosing to its levels in plasma and CSF, and what effect these have on other biochemical processes and finally to the treatment of depression.

## Honors and Awards:

None

## Publications:

None

| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CI 05012-01 PHAR |
|---|---|---|

PERIOD COVERED
October 1, 1979 - September 30, 1980

TITLE OF PROJECT (80 characters or less)

Pharmacokinetics of Thiopental Sodium in Hyperthermia Patients

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Michael Dubois, Anesthesiology

Dulal C. Chatterji, Ph.D., Pharmacy Dept.

Raymond F. Greene, M.S., Pharmacy Dept.

COOPERATING UNITS (if any)

Anesthesiology

LAB/BRANCH
Pharmaceutical Development Service

SECTION

INSTITUTE AND LOCATION
CC, NIH, Bethesda

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 0.4 | 0.3 | 0.1. |

CHECK APPROPRIATE BOX(ES)

x (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Pharmacokinetics of thiopental sodium in patient undergoing Hyperthermia treatment was studied to understand why these patinets need an unusually large dose of the sedative. HPLC-methods were developed to assay pentothol in plasma and its metabolite in urine. The results suggest that the plasma levels of thiopental in hyperthermia patients are within normal range in spite of the high dose, there is no unusual increase in the metabolism and drug levels stay high even after 24 hr. of dosing, all suggesting that the drug gets shunted into far reservoirs in the body during hyperthermia.

Serial No. Z01 05012-01 PHAR
Pharmacy Department
Clinical Center
Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1979 - September 30, 1980

Project Title: Pharmacokinetics of Thiopental in Hyperthermia Patients.

Previous Project Number: None

Principal Investigator: Michael Dubois, M.D.

Other: Dulal C. Chatterji, Ph.D., Pharmacy Dept.
Raymond F. Greene, M.S., Pharmacy Dept.

Cooperating Unit: Anesthesiology

Man Years: Total: 0.4
Professional: 0.3
Other: 0.1

## Project Description

### Objective:

To study the disposition of thiopental in patients undergoing hyperthermia treatment.

### Methods Employed:

Blood samples were collected from patients sedated with thiopental and undergoing hyperthermia treatment. Urine samples were either collected via catheter or by normal voiding. The samples were analyzed for thiopental and its major metabolite, thiopental carboxylic acid, by HPLC.

### Major Findings:

It was found that in spite of a much larger dose of thiopental given, the blood levels during the infusion remain within the normal range, but after that levels persist at about 2-3 times higher than would be expected of a normothermic subject. The metabolism of the drug during infusion was not unusually high and it was therefore concluded that the drug is being shunted to fat reservoir in the body during hyperthermia.

### Significance to the Biomedical Research:

The project provided valuable information on the pharmacokinetics of fat soluble drugs in febrile patients.

Proposed Course:

Study the metabolism and excretion of thiopental in greater detail to get an insight into the changes in physiological functions during elevated body temperatures.

Honors and Awards:

None

Publications:

None

October 1, 1979 through September 30, 1980

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

DEPARTMENT OF REHABILITATION MEDICINE

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October 1, 1979 through September 30, 198

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

## DEPARTMENT OF REHABILITATION MEDICINE

### I. Departmental Missions and Goals

The primary mission of the Department of Rehabilitation Medicine is to provide the highest quality physiatric evaluation and treatment, physical therapy, occupational therapy, and speech therapy for Clinical Center patients referred by Institute physicians, and to develop indices to evaluate these services.

An equally important mission of the Department is to support efforts of and collaborate with Institute physicians engaged in research relevant to physical medicine rehabilitation.

The third mission is to initiate both clinical and basic research independent of the Institutes in the rehabilitation of mentally and physically handicapped individuals.

A fourth mission is to advocate and defend the rights of handicapped persons, and to use education, prevention, and legislation to accomplish this goal.

The fifth mission is to increase dialogue between NIH Department of Rehabilitation Medicine and other academic and community facilities concerned with care of the handicapped.

### II. Departmental Activities

A. Staffing pattern is presented in Addendum I.

B. Patient Care Statistics

Patient care statistics are presented in detail in Tables 1-2 for Physical Therapy, 3-4 for Occupational Therapy, 5-6 for Speech Therapy, and Table 7 for Physiatrists.

### III. Major Progress

A. Patient Care and Professional Services

1. Occupational Therapy Section

a. Standardization of patient care has been effected in several areas to provide quality care more uniformly and to evaluate the impact of occupational therapy on treatment outcome. In the Occupational Therapy Physical Disabilities program and newly revised Activities of Daily

Living Evaluation and the new Upper Extremity Functional Evaluation may be used to measure changes in function and more sharply define areas of dysfunction. In the Occupational Therapy Mental Health program, the initial evaluation will assure consistent evaluation on all 5 National Institute of Mental Health Nursing units.

b. The Occupational Therapy Mental Health Work Therapy program has been broadened to include patients with physical disabilities. Prevocational evaluation has been added to this program by the consultant rehabilitation counsellor, Martha Bernad.

c. A Patient Education Group to teach joint protection and energy conservation to patients with rheumatoid arthritis has been established and is well received by the patients and the professional staff.

2. Physical Therapy Section

a. After completion of a cooperative effort designed to evaluate optimal post-operative rehabilitation of the patient undergoing axillary dissection, it was noted that we were providing better care for these patients; not only did they achieve better shoulder range, but they also had shorter hospital stays than did historical controls. Standardization of evaluation indices for patients with soft tissue sarcoma are now routinely used and provide valuable baseline data about strength, range of motion and function. In longitudinal studies we will determine which treatments are most effective for this patient group as well as learn how to correlate strength and range with function.

b. Increased service to patients with foot-related problems was initiated by Mr. Joseph K. Reed, Jr. The entire physical therapy staff has been trained to provide this care through inservice education. The evaluation of and prescription for problems are departmental activities; the fabrication to specification, is performed by a private company.

3. Speech Pathology Section

a. An increasing number of inpatients has been referred for speech pathology in the past year. Much effort has gone into providing proper evaluation of cognitive function, utilizing sophisticated measures of memory and ability to process new information.

4. General Departmental Services

a. Temperature biofeedback and training in relaxation techniques are offered to all NIH patients referred for treatment of Raynaud's phenomenon.

b. The design and use of temporary hemipelvectomy and hip disarticulation prosthesis are available within 10 working days of suture removal or surgeon approval in patients undergoing those procedures. One prototype, using ultralite plastic, has reduced the weight of the prosthesis by several pounds.

B. Research

1. The Occupational Therapy Service, Physical Disabilities Program, has provided quantitative functional evaluation of patients being recalled with a diagnosis of juvenile rheumatoid arthritis.

2. Summary of advances in several areas of research are presented:

a. Fourteen patients with above-knee amputation for osteogenic sarcoma had femur length of less than 2" distal to the lesser trochanter. While standard teaching suggests they be treated as high disarticulations and fitted with such a prosthesis, we electd to treat them as above-knee amputees using polycentric knee and pelvic bands, 7 of the 11 still living are using their limbs more than 8 hours a day.

b. The functional outcome of 31 patients with soft tissue sarcoma of the extremities who underwent wide excision of the involved muscle group(s) and 3800-7000 rads of radiation was determined. Those with lower extremity lesions, as opposed to upper extremity or trunkal lesions, had significant morbidity and disability as defined by loss of range of motion, strength and lower scores in assessing Activity of Daily Living.

c. A real-time ultrasonic imaging system has been developed to visualize dynamic motion of the tongue during continuous speech. Lingual motion configurations are displayed and recorded synchronously with the audible voice, an averaged audio signal, time in milliseconds, and frontal and lateral views of the face during articulation. Data on the amplitude changes of the tongue surface and duration of the production of selected phonemes was obtained on 30 normal adults. This technique provides a reliable reproducible and non-invasive technique for quantifying tongue motion.

d. The role and timing of physical therapy following axillary dissection was studied in a prospective randomized clinical trial. Patients received early (day 1) or delayed (day 7) range of motion following surgery. Those patients who received early shoulder motion had significantly more wound drainage and remained in hospital longer than did those whose range of motion was delayed. Early shoulder range, especially abduction and flexion, has an adverse effect on wound healing and drainage.

e. Sixty-six patients with psoriatic arthritis were evaluated clinically for severity of disease and subtype of arthritis. These were then correlated with certain human lymphocyte antigen frquencies. Patients with severe arthritis were distinguighable from those with mild or moderate disease as were those with several subtypes of arthritis.

3. Publications

a. Healing of Peptic Ulcers During Continuing Anti-Inflammatory Drug Therapy in Rheumatoid Arthritis, LH Gerber, PJ Rooney, DM McCarthy, Journal of Clinical Gastroenterology, in press.

b. Leg Function After Radiotherapy for Ewings Sarcoma, K Jentzsch, H Binder, H Cramer, DL Glaubiger, RM Kessler, C Bull, TC Pomeroy, NL Gerber, Cancer, in press.

c. HLA Alloantigens in Psoriasis and Psoriatic Arthritis: Evidence for the Influence of Multiple Genes in the Major Histocompatibility Complex, C Murray, DL Mann, LH Gerber, W Barth, S Perlman, JL Decker, TP Nigra, Journal of Clinical Investigation, in press.

d. Principles in the Rehabilitation of Patients with Rheumatic Disease, LH Gerber in Textbook of Rheumatology, eds. Kelley, Sledge, Harris, W. B. Saunders, Philadelphia, 1980.

C. Training

1. Weekly inservice education has been administered by occupational therapy and physical therapy staff and has reflected their interests.

2. Bi-monthly journal club for the medical staff, organized around current interests of the multidisciplined professionals has been ongoing.

3. The staff has remained active in extramural training programs including:

a. USPHS Specialty Section Meetings
b. George Washington University
c. Sibley Hospital Medical Staff
d. Washington Hospital Center
e. Downstate Medical Center

4. Core curriculum requirements have been met by all occupational therapy staff.

5. Many staff members have participated in interagency conferences and committees including: American Speech and Hearing Association, Veterans Administration, National Arthritis Advisory Board, National Institutes for Handicapped Research.

D. Administrative

1. Monthly staff meetings including Chiefs of Occupational Therapy and Physical Therapy, Speech Pathologist, and all physicians have been ongoing in order to develop a policy and procedure manual which describes all aspects of departmental activity. A definition of Rehabilitation Medicine and departmental procedures has been accomplished so far. We are currently developing quality assurance standards.

2. Coordination with George Washington University has resulted in the assignment of a 3rd year Physical Medicine and Rehabilitation resident to the Department of Rehabilitation Medicine.

## IV Future Objectives

### A. Patient Care and Professional Services

1. Establish better communications with Institute physicians in order to better coordinate service to inpatients and outpatients and to better inform physicians of rehabilitation activities.

2. Develop and expand multidisciplinary patient care conferences with nursing and social service in order to provide discharge planning where appropriate.

3. Develop criteria for standards of practice for occupational therapy, physical therapy, speech and physical medicine for inclusion in the Policy and Procedure Manual of the Department.

4. Design and implement a biomechanics section that will provide clinically relevant information about motion.

5. Expand, refine and validate assessment forms of upper extremity function, higher cortical function, task performance for mental health occupational therapists.

6. Develop concept of health promotion as part of patient education program within rehabilitation.

### B. Research

1. Establish capability for studying biomechanics of hand function.

2. Establish capability for studying biomechanics of motion in hip disarticulation amputees.

3. Application of ultrasound as a biofeedback tool in treating patients with oral motor dysfunction will be assessed.

### C. Training

1. General staff familiarity with computer applicability to Department of Rehabilitation Medicine needs will be sought through inservice training.

2. Increased facility with new orthotic design and fabrication will be encouraged for all occupational and physical therapy staff.

## Addendum I - Department of Rehabilitation Medicine Staffing Pattern

### Office of the Chief

| | | |
|---|---|---|
| Chief, Department of Rehabilitation Medicine | 1 | |
| Assistant Chief | 1* | |
| General Medical Officer | 1 | |
| Secretaries | 3 | (1 part-time) |
| | 6 | |

### Physical Therapy Service

| | |
|---|---|
| Chief, Physical Therapy Service | 1 |
| Assistant Chief | 1 |
| Staff Physical Therapists | 5 |
| Physical Therapy Assistants | 2 |
| | 9 |

### Occupational Therapy Service

| | | |
|---|---|---|
| Chief, Occupational Therapy Service | 1 | |
| Deputy Chief | 1 | |
| Staff Occupational Therapists | 6+ | (2 part-time) |
| | 8 | |

### Speech Therapy Service

| | |
|---|---|
| Speech Pathologist | 1 (part-time) |

* Now recruiting for Assistant Chief, Department of Rehabilitation Medicine position.

## PHYSICAL THERAPY SERVICE

Table 1: Statistical Report Fiscal Year 1980
October 1, 1979 to September 30, 1980

| Institute | Number of Patients Treated FY 80 | | Number of Patient Visits FY 80 | |
|---|---|---|---|---|
| | IP | OP | IP | OP |
| NCI | 677 | 521 | 4020 | 2792 |
| NEI | 12 | -- | 9 | 1 |
| NHBLI | 80 | 33 | 636 | 181 |
| NIAID | 131 | 11 | 688 | 68 |
| NIAMDD | 267 | 154 | 1221 | 1373 |
| NICHD | 97 | 7 | 159 | 1 |
| NIDR | 4 | -- | 56 | 0 |
| NIMH | 126 | 3 | 648 | 6 |
| NINCDS | 434 | 67 | 2873 | 424 |
| TOTAL | 1,828 | 796 | 10,310 | 4,846 |

## PHYSICAL THERAPY SERVICE

### Table 2: Comparative Statistics Fiscal Years 1975 - 1980

| Fiscal Year | Number of Patients Treated | | Number of Patient Visits | |
|---|---|---|---|---|
| | IP | OP | IP | OP |
| 1975 | 1,694 | 586 | 12,960 | 2,071 |
| 1976 | 2,085 | 796 | 9,016 | 2,155 |
| 1977* | 2,615 | 966 | 11,513 | 2,621 |
| 1978 | 1,726 | 631 | 9,569 | 3,160 |
| 1979 | 1,948 | 716 | 10,563 | 4,048 |
| 1980 | 1,828 | 796 | 10,310 | 4,846 |

* Figures for FY 1977 represent 15-month totals because transitional quarter is included.

## OCCUPATIONAL THERAPY SERVICE

Table 3: Summary Reporty by Institute of Number of Patients Treated, Number of Treatment House*
Fiscal Year - 1980

| Institute | Number of Patients Treated | | Number of Patient Treatments | |
|---|---|---|---|---|
| | IP | OP | IP | OP |
| NCI | 135 | 89 | 545 | 413 |
| NEI | 1 | -- | 3 | -- |
| NHLBI | 15 | 4 | 110 | 9 |
| NIAID | 41 | 5 | 162 | 14 |
| NIAMDD | 185 | 210 | 337 | 658 |
| NICHD | 18 | 22 | 48 | 57 |
| NIDR | 2 | -- | 26 | 0 |
| NIMH | 251 | 1 | 9459 | 1 |
| NINCDS | 285 | 53 | 1631 | 192 |
| TOTAL | 933 | 384 | 12,321 | 1,344 |

## OCCUPATIONAL THERAPY SERVICE

Table 4: Comparative Statistics
Fiscal Years 1975 - 1980

| Fiscal Year | Number of Patients Treated | | Number of Patient Visits | |
|---|---|---|---|---|
| | IP | OP | IP | OP |
| 1975 | 1,220 | 359 | 10,622 | 358 |
| 1976 | 1,411 | 235 | 12,052 | 599 |
| 1977* | 1,774 | 294 | 14,595 | 519 |
| 1978 | 1,326 | 153 | 13,704 | 609 |
| 1979** | 893 | 388 | 11,872 | 1,550 |
| 1980 | 933 | 384 | 12,323 | 1,344 |

* Estimates for July-September, 1979

** Figures for FY 1977 represent 15-month totals because transitional quarter is included.

## SPEECH THERAPY SERVICE

### Table 5: Comparative Statistics Fiscal Year 1980

| Fiscal Year | Number of Patient Treatments | | Number of Treatment Hours | |
|---|---|---|---|---|
| | IP | OP | IP | OP |
| 1977 | 228 | 143 | 456 | 286 |
| 1978 | 361 | 311 | 626 | 597 |
| 1979* | 338 | 350 | 652 | 690 |
| 1980 | 484 | 266 | 753 | 447 |

* July, August, and September 1979 estimated

## SPEECH THERAPY SERVICE

Table 6: Summary Report by Institute of Number of Patients Treated, Number of Treatment Hours Fiscal Year 1980

| Institute | Number of Patient Treatments | | Number of Treatment Hours | |
|---|---|---|---|---|
| | IP | OP | IP | OP |
| NCI | 58 | 25 | 82 | 55 |
| NHBLI | 49 | 49 | 98 | 60 |
| NIAID | 33 | 6 | 70 | 12 |
| NIAMDD | 20 | 13 | 50 | 26 |
| NICHD | 25 | 68 | 50 | 134 |
| NIDR | -- | 3 | -- | 6 |
| NIMH | 89 | 1 | 89 | 2 |
| NINCDS | 210 | 92 | 314 | 134 |
| NEI | -- | -- | -- | -- |
| COURTESY | -- | 9 | -- | 18 |
| SUBTOTAL | 484 | 266 | 753 | 447 |
| TOTAL | 750 | | 1,200 | |

DEPARTMENT OF REHABILITATION MEDICINE

OFFICE OF THE CHIEF

Table 7: Number of Patient Evaluations by Physiatrists
Fiscal Years 1975 - 1980

| Fiscal Year | Total |
|---|---|
| 1975 | 897 |
| 1976 | 848 |
| 1977 | 1,625 (15 mos) |
| 1978 | 2,750 (12 mos)* |
| 1979 | 2,779 |
| 1980 | 2,667 |

* Additional physician added to staff 8/77

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>**NOTICE OF**<br>**INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 06001-04 REHAB |

PERIOD COVERED
November, 1976 through June, 1979

TITLE OF PROJECT (80 characters or less)
Correlation of Activity of Psoriatic Arthropathy with Psoriasis in Patients Receiving PUVA (Psoralen Ultraviolet A Therapy)

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

N. L. Gerber, M. D., Chief, Department of Rehabilitation Medicine, CC
Werner Barth, M. D., Washington Hospital Center (off site)
John L. Decker, M. D., ARB, NIAMDD
A. Eric Jones, M. D., Nuclear Medicine, CC
T. Nigra, M. D., Washington Hospital Center
Susan Perlman, M. D., Washington Hospital Center

COOPERATING UNITS (if any)
Washington Hospital Center, Rheumatology & Dermatology Section
Nuclear Medicine

LAB/BRANCH
Arthritis & Rheumatism/Rehabilitation Department, CC

SECTION

INSTITUTE AND LOCATION
NIAMDD/CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1 | 2/3 | |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

PUVA Therapy is recognized as an effective mode in treating psoriasis. It has no known anti-rheumatic properties. Approximately 15% of patients with psoriasis nave an associated arthritis. This study monitors arthritis activity in patients with psoriatic arthritis during the course of PUVA Therapy, and correlates it with skin response to PUVA. Data shows two subpopulations of patients with arthritis: those with peripheral joint and those with axial involvement. The former group demonstrates a positive correlation between skin responsiveness and joint responsiveness. The latter group do not. The latter group has sacroilliitis and appears refractory to most forms of anti-inflammatory medication.

Project No. Z01 CL 06001-04 REHAB
1. Rehabilitation Department
2. Clinical Center
3. Bethesda, Maryland

PHS-NIH
Individual Project Report

Project Title: Correlation of Activity of Psoriatic Arthropathy with Psoriasis in Patients Receiving PUVA (Psoralen Ultraviolet A Therapy)

Previous Serial Number: Z01 CL 06001-03 REHAB

Principal Investigator: N. L. Gerber, M. D.

Cooperating Units: Washington Hospital Center, Department of Dermatology and Rheumatology
Diagnostic Imaging Section, CC

Man Years: Total 1
Professional 2/3

## Project Description

### Objectives

Patients with psoriasis and psoriatic arthritis receiving photochemotherapy according to the Oral Methoxsalen-Photochemotherapy Cooperative Clinical Protocol (PUVA) have been followed to determine the effect of PUVA on skin and joint disease, and to determine if a correlation exists between skin and joint activity.

### Materials and Methods

All were treated with PUVA until skin clearing (95%) and were then placed on maintenance PUVA schedules. Assessment at regular intervals included % psoriatic skin, articular index of peripheral and root joints (AI), visual analog scale, baseline x-rays and serial joint scans.

Twenty-seven patients have been followed. They were later subdivided into 2 groups: 21 with asymmetric seronegative peripheral arthritis (P) and 6 with active peripheral joint disease meeting New York Criteria for ankylosing spondylitis (S). S and P subgroups have been followed for a mean of 69 and 29 weeks, respectively. P had a higher initial AI (60 vs 50), but S had greater % skin involved (52 vs 39), longer duration of psoriasis (22 vs 16 yrs). 6/6 and 18/21 P cleared skin on PUVA. In contrast, mean % improvement in AI after initial skin clearing was 16% for S vs 49% for P. After first skin clearing, there were 10 skin flares per 280 patient-weeks in S receiving maintenance PUVA vs 2 skin flares per 171 patient-weeks in P. For these two P patients, joint flares were temporally related to skin flares. S skin and joint activity appeared to vary independently.

## Significance to Biomedical Research

This study suggests there are at least 2 clinical subgroups of patients with psoriatic arthritis and each responds differently to control of underlying skin disease. For P skin clearing is associated with significant improvement in arthritis. For patients with S, the course of skin and joint disease varies independently.

| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 06005-03 REHAB |
|---|---|---|

PERIOD COVERED
February 1977 through June, 1979

TITLE OF PROJECT (80 characters or less)

Biofeedback in the Management of Raynaud's Phenomenon

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

N. L. Gerber, M. D., Chief, Rehabilitation Department, CC
Cynthia Smith, OTR, Occupational Therapy Service, CC
Tim Reyburn, OTR, Occupational Therapy Service, CC
Andy Novick, RPT, Physical Therapy Service, CC
Elaine Bardo, OTR, Occupational Therapy Service, CC

COOPERATING UNITS (if any)

LAB/BRANCH

SECTION
Rehabilitation Department

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 3/5 | 1/5 | |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Patients with primary or secondary Raynaud's phenomenon were randomized to receive relaxation training or temperature biofeedback in an attempt to relieve symptoms of Raynaud's phenomenon and control the temperature of the distal digits. Patients were monitored for skin temperature during training sessions, and placed in a 38°F room with constant temperature monitoring. Post-training, patients were able to control temperature better and keep hands warmer in ambient outdoor temperature and in the cold room. Both groups of patients did equally well in terms of control of temperature and in areas of symptom control.

Project No. Z01 CL 06005-03 REHAB
1. Rehabilitation Department
2. Clinical Center
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1977 through June, 1979

Project Title: Biofeedback in the Management of Raynaud's Phenomenon

Previous Project No.: Z01 CL 06005-02 REHAB

Principal Investigator: N. L. Gerber, M.D.

Others: Cynthia B. Smith, OTR, Occupational Therapy Service, CC
Tim Reyburn, OTR, Occupational Therapy Service, CC
Andy Novick, RPT, Physical Therapy Service, CC
Elaine Bardo, OTR, Occupational Therapy Service, CC

Man Years: Total -
Professional -

## Project Description

This study was designed to evaluate the efficacy of autogenic training in the management of Raynaud's phenomenon. Biofeedback has been demonstrated effective in control of cardiac arrhythmias, bowel incontinence and other autonomic functions. Its efficacy in management of Raynaud's remains unproven.

Because little is known about the kinetics of response of skin temperature to cold, a further objective is to evaluate the normals response to 38°F cold and compare it to the Raynaud's patient.

## Materials and Methods

Twenty patients, with primary or secondary Raynaud's phenomenon, who demonstrated white/blue/red color change when placed at 38°F for three minutes, were selected for study. Each was randomly assigned to receive temperature biofeedback or relaxation techniques. All had 20 hours of training, kept accurate logs of their Raynaud's attacks, and were reevaluated after training.

## Major Findings

All patients completed training. In the laboratory, 19 patients raised their skin temperature consistently during final 5 training sessions with an average increase of 6°F. Average digital temperature of 74°F increased from pre-training level of 77°F (68°-87°) to 84°F (77°-92°) post-training; and at 38° for 3 minutes increased from 66°F to 71°F.

Post-training, 19 did not develop the 3-color change after 3 minutes at 38°F. A significant change in kinetics of skin temperature at 38°F was noted. Prior to training, patients with Raynaud's phenomenon would drop 10°F within one minute of entering the 38°F cold room. Post-training, the temperature drop was 8°F over a 3-minute period, thus appoximating the normals' response to cold.

| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 06006-02 REHAB |
|---|---|---|

PERIOD COVERED
October 1978 through June 1979

TITLE OF PROJECT (80 characters or less)

The Diagnostic Capabilities of Ultrasound in Conditions Causing Oral-Motor Dysfunction

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

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Thomas H. Shawker, M. D., Diagnostic Radiology, CC
Thomas E. Hall, M.S., DRS:BEI
Willard C. Whitehouse, B.S, OCRI:CC
Lynn H. Gerber, M. D., Rehab:CC
Stephen B. Leighton, ScD., R:BEI

COOPERATING UNITS (if any)

BEI, Diagnostic Radiology, T.V. Engineering

LAB/BRANCH

SECTION
Department of Rehabilitation Medicine, CC

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1/5 | 1/7 | |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

It has been difficult to correlate clinical impressions of oral-motor dysfunction and tongue function without using invasive procedures. A real-time with ultrasonic imaging system using a B-scan mechanical sector with simultaneous audio and video signals was developed to evaluate the range of tongue motions used during speech articulation. Thirty normal subjects were studied to obtain normalized tongue configuration graphs and durational data on production of selected phonemes. Measures of amplitude and velocity of tongue motions on these phonemes is being determined. Preliminary results indicate that ultrasound provides a reliable pattern of tongue movement in normals. Patients with amyotrophic lateral sclerosis and polymyositis will be studied to establish a continuum of oral motor function to differentiate between normal and impaired speech mechanisms.

Project No. Z01 CL 06006-02 REHAB
1. Rehabilitation Department
2. Clinical Center
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
October 1, 1978 through June, 1979

Project Title: The Diagnostic Capabilities of Ultrasound in Conditions Causing Oral-Motor Dysfunction

Previous Project No.: Z01 CL 06006-01 REHAB

Others: Thomas H. Shawker, M. D.
Thomas E. Hall, M.S.
Willard C. Whitehouse
Lynn H. Gerber, M. D.
Stephen B. Leighton, ScD

Man Years: Total - 1/5
Professional - 1/7

## Project Description

### Objectives

(1) To compare and evaluate tongue movement in normal and neurologically impaired subjects using ultrasonic imaging with simultaneous audio and video tape recording of phonemes selected to represent the range of tongue motion during articulation. The performance of patients with ALS, a neuromotor dificit, will be compared to that of patients with polymyositis who have myopathy; (2) To establish a continuum of oral-motor function for use in clinical examination; (3) To determine whether ultrasonic imaging of oral performance is sufficiently sensitive to detect progressive changes in oral-motor function.

### Material and Methods

Thirty normal subjects ages 25 to 65 who did not have obvious speech or dental impairment were evaluated using ultrasonic imaging of tongue motion during the production of 5 phonemes spoken singly and in various combinations. Subjects were seated in an appropriately designed wheelchair with a headrest and mirrors. A specially constructed ultrasonic transducer was positioned manually behind the mental symphysis of the mandible in the median sagittal plane. Simultaneous front and side views of the subject's face were monitored through the mirrors mounted on the chair. All stimuli and responses were recorded on video tape for later analysis. Signals were recorded both visually and auitorially. Normalized tongue configuration graphs are being derived for each phoneme using a stop-frame analysis of each phoneme. The amplitude and velocity of the tongue

during production of phonemes is being obtained. We plan to evaluate 15 patients.

## Major Progress

A non-invasive, reliable method for studying oral-motor functions using a real-time ultrasonic imaging system has been developed cooperatively with diagnostic radiology, biomedical and television engineering. This unique system produces simultaneous auditory and visual signals which correlate with tongue motions during speech production. Thirty normal subjects have been evaluated to determine a baseline of lingual performance from which to compare patients with neurologic and motor dysfunction. It appears that this system will have significant diagnostic capabilities.

| SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT | PROJECT NUMBER<br>Z01 CL 06007-02 REHAB |
|---|---|---|

PERIOD COVERED
February 1979 through July 1979

TITLE OF PROJECT (80 characters or less)
Oxygen Consumption and Energy Expenditure in Hemipelvectomy and Hip Disarticulation Amputees

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

Farhad Nowroozi, M. D.
Lynn H. Gerber, M. D.
Mario Salvanelli, RPT

COOPERATING UNITS (if any)

None

LAB/BRANCH

SECTION
Department of Rehabilitation Medicine,

INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1/5 | 1/10 | |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

This study is designed to assess: (1) comfortable speed of walking (CSW), and (2) energy expenditure and oxygen consumption of high level lower extremity amputees (hip disarticulation and hemipelvectomy) during ambulation with or without prosthesis, and also at rest, breathing room air. Other parameters such as respiratory exchange ratio, etc., will also be calculated. These respiratory and metabolic measurements will be measured in a group of normal individuals age and sex matched.

Project No. Z01 CL 06007-02 REHAB
1. Rehabilitation Department
2. Clinical Center
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
February, 1979 through July, 1979

Project Title: Oxygen Consumption and Energy Expenditure in Hemipelvectomy and Hip Disarticulation Amputees

Previous Project No. Z01 CL 06007-01 REHAB

Principal Investigator: Farhad Nowroozi, M.D.

Other Participants: Lynn H. Gerber, M. D.
Mario L. Salvanelli, RPT

Man Years: Total - 1/5
Professional - 1/10

## Project Description

### Objectives

This study is designed to assess: (1) comfortable speed of walking (CSW), and (2) energy expenditure and oxygen consumption of high level lower extremity amputee (hip disarticulation and hemipelvectomy) during ambulation with or without prosthesis and also at rest, breathing room air. Other parameters such as respiratory exchange ratio, etc., will also be calculated. These respiratory and metabolic measurements will be measured in a group of normal individuals age and sex matched.

### Materials and Methods

CSW in high level of amputation will be measured by asking the patient to walk 4 X 100 meters at their comfortable speed while breathing through mouthpiece with nose clip on. Metabolic and respiratory parameters will be measured after 15 minutes rest, walking at CSW, fastest speed walking (FSW), slowest speed of walking (SSW) while wearing the prosthesis and breathing through mouthpiece. These parameters will also be measured while the patients are walking without prosthesis, but with 2 crutches. Post-exercise measurements will be then carried out.

### Major Findings

None. Study in process at the present time; insufficient data to report.

| | | |
|---|---|---|
| SMITHSONIAN SCIENCE INFORMATION EXCHANGE<br>PROJECT NUMBER (Do NOT use this space) | U.S. DEPARTMENT OF<br>HEALTH, EDUCATION, AND WELFARE<br>PUBLIC HEALTH SERVICE<br>**NOTICE OF**<br>**INTRAMURAL RESEARCH PROJECT** | PROJECT NUMBER<br>Z01 CL 06008-02 REHAB |

PERIOD COVERED
January 1, 1979 through January, 1980

TITLE OF PROJECT (80 characters or less)

A Randomized Prospective Study of the Effect of Early Versus Delayed Physical Therapy in the Patient Undergoing Axillary Dissection

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

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Michael Lotze, M.D., Surgery Branch, CT, NCI
Lynn H. Gerber, M.D., Department of Rehabilitation Medicine, CC
Mary Duncan, RPT, Department of Rehabilitation Medicine, CC
Farhad Mowroozi, M. D., Department of Rehabilitation Medicine, CC

COOPERATING UNITS (if any)

None

LAB/BRANCH

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INSTITUTE AND LOCATION
CC, NIH, Bethesda, Maryland 20205

| TOTAL MANYEARS: | PROFESSIONAL: | OTHER: |
|---|---|---|
| 1 1/2 | 1 1/2 | |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

Patients with melanoma or breast carcinoma undergoing axillary dissection are randomized to receive early or delayed shoulder mobilization following surgery. The study is designed to answer two questions: does Physical Therapy immediately post-op. interfere with wound healing; does Physical Therapy immediately post-op. offer more effective treatment for shoulder function in this population. Eighteen patients have been entered into the study, but data is not yet definitive.

Project No Z01 CL 06008-02 REHAB
1. Rehabilitation Department
2. Clinical Center
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
January, 1979 through January, 1980

Project Title: A Randomized Prospective Study of the Effect of Early Versus Delayed Physical Therapy in the Patient Undergoing Axillary Dissection

Previous Project No.: Z01 CL 06008-01 REHAB

Principal Investigator: Steven A. Rosenberg, M.D.

Other Participants:
Michael Lotze, M. D.
Lynn H. Gerber, M. D.
Mary Duncan, RPT
Farhad Nowroozi, M. D.

Man Years:
Total 1 1/2
Professional 1 1/2

## Objectives

This protocol is designed to answer two basic questions (1) Does physical therapy immediately postoperatively interfere with wound healing? (2) Is immediate postoperative physical therapy more effective in rehabilitating the axillary dissection patient than a program that is less vigorous and delayed until wound healing is more progressed?

## Materials and Methods

All patients about to undergo axillary dissection for either melanoma of the upper extremity or upper torso and those patients about to undergo modified radical mastectomy with lymph node dissection will be eligible for this study. Patients who have preexisting conditions that would affect their neck or shoulder function are not eligible for the protocol.

Following initial outpatient evaluation and assessment of suitability for inclusion in the axillary dissection protocol, patients who agree to enter this study will be randomized into either vigorous or conservative physical therapy groups.

Stratification will be done for (1) Age - greater or less than 50 years, (2) Tumor type, primary melanoma versus breast carcinoma.

Major Findings: Inadequate data.

Significance to Biomedical Research:

This study will help answer the questions of how best to rehabilitate patients undergoing axillary dissection.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)

U.S. DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NOTICE OF
INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 CL 06009-02 REHAB

PERIOD COVERED
June 1978 through June, 1981

TITLE OF PROJECT (80 characters or less)

Intravenous Cyclophosphamide in the Treatment of Rheumatoid Arthritis

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

John H. Klippel, M. D., ARB, NIAMDD
John L. Decker, M. D., ARB, NIAMDD
Jacob Karsh, M. D., ARB, NIAMDD
Paul Plotz, M. D., ARB, NIAMDD
Lynn H. Gerber, M.D., Rehabilitation Medicine, CC

COOPERATING UNITS (if any)

LAB/BRANCH
Arthritis & Rheumatism Branch/Rehabilitation Medicine, CC

SECTION

INSTITUTE AND LOCATION
NIAMDD/CC, NIH, Bethesda, Maryland 20205

| | | |
|---|---|---|
| TOTAL MANYEARS:<br>1/5 | PROFESSIONAL:<br>1/5 | OTHER: |

CHECK APPROPRIATE BOX(ES)

☒ (a) HUMAN SUBJECTS ☐ (b) HUMAN TISSUES ☐ (c) NEITHER

☐ (a1) MINORS ☐ (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords)

The efficacy of intravenous cyclophosphamide in the treatment of rheumatoid arthritis is to be evaluated. Patients are randomly assigned cyclophosphamide or placebo, and are evaluated for disease activity using clinical, functional and serological assessments. To date only 6 patients have been entered into the study.

Project No. Z01 CL 06009-02 REHAB
1. Rehabilitation Department
2. Clincial Center
3. Bethesda, Maryland

PHS-NIH
Individual Project Report
June, 1978 through June, 1981

Project Title: Intravenous Cyclophosphamide in the Treatment of Rheumatoid Arthritis

Previous Project No.: Z01 CL 06009-01 REHAB

Principal Investigator: John H. Klippel, M. D.

Other Participants:
John L. Decker, M. D.
Jacob Karsh, M. D.
Paul Plotz, M. D.
Lynn H. Gerber, M. D.

Man Years: Total - 1/5
Professional - 1/5

## Project Description

We propose to evaluate the therapeutic efficacy and toxicity of intravenous cyclophosphamide given at 2-month intervals in the treatment of patients with rheumatoid arthritis.

## Materials and Methods

This study will be a double-blind trial of 4 infusions of either intravenous cyclophosphamide (1 gram per meter squared, or less) or saline to be given at 2-month intervals for 6 consecutive months.

Patients will be assigned to a treatment group according to a randomized schedule allocating 10 patients with rheumatoid arthritis who satisfy the admissin criteria into each of the 2 treatment groups.

For each patient entering the study, a study coordinator and study observer will be assigned from among the study investigators. The responsibilities of these persons for the entire duration of the study for that patient are as follows:

1. Study coordinator:
    a. determine and order each dose of medication
    b. record side effects observed during the study

2. Study observer:
   a. perform and record the results of all clinical assessments; these observations will be made without knowledge of hematologic studies or symptoms developing during the study.

## Major Findings

Inadequate data collected to date.

## Significance to Biomedical Research

This study attempts to determine toxicity and efficacy of periodically administered cyclophosphamide in patients with rheumatoid arthritis. Additional information may be obtained with respect to evaluation of patients and correlation of clinical, functional, and serological parameters.

October 1, 1979 through September 30, 1980

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH
DUMMARY OF ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

## SOCIAL WORK DEPARTMENT

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October 1979 through June 1980

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October 1979 through June 1980

October 1, 1979 through September 30, 1980

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

# SUMMARY OF ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

## SOCIAL WORK DEPARTMENT

## I. DEPARTMENT MISSIONS AND GOALS

The overall mission of the Social Work Department is to provide wide-range social services to biomedical research patients and simultaneously to reinforce rapport between the investigative/therapeutic systems and the patient/family systems.

## II. DEPARTMENT ACTIVITIES

### Staffing Patterns

As the Social Work Department entered its 27th year, the seventh Chief of the Department was appointed effective June 1, 1980. At the close of FY 1980, the professional staff position assignments were as follows:

Professional Positions

| Position Breakdown | Full-Time | Part-Time |
|---|---|---|
| Office of the Chief | 2 | 0 |
| Program Supervisors | 2 | 0 |
| Social Work Sections | | |
| Cancer | 5 | 2 |
| Child Health and Human Development | 0 | 1 |
| Heart, Lung and Blood | 2 | 1.5 |
| Arthritis, Metabolism and Digestive Diseases | 1 | 1 |
| Allergy and Infectious Diseases | 1 | 0.5 |
| Neurological and Communicative Disorders and Stroke/Eye | 2 | 0 |
| | 15 | 6 |

Section staff changes included one resignation from a permanent part-time position, one maternity leave from a permanent full-time position, and one 6-month White House detail assignment from a permanent full-time position. Two temporary positions, one full-time, and one part-time, compensated for these reductions-in-staff. Additionally, four social work representatives were employed during the Summer 1980.

## Administrative Components

Throughout this reporting period, the Social Work Department remained under Clinical Center Administrative study. From the perspective of a social psychologist, the Department was examined for effects of its organizational dynamics, management objectives, and mission statements. In February 1980, the Department was evaluated by an On-Site Advisory Committee of four recognized social workers. On a two-day assignment, this Committee surveyed the structure, methods, mission, goals, and other critical elements of departmental operation and function.

This year of reflection was productive for analysis of problems and guidelines for solutions. The Department's mission and philosophy were found in need of revision for providing operational direction. There was reemphasis on the merits of documentation for accountability to the patient, the Clinical Center Administration, the Social Work Department, the profession, and for the provider social worker. Information systems were recommended for assurance of quality and quantity of social services, for provision of source material for social work research, and for facts supportive of directions for staff and program development.

Members of the Department became involved with the importance of quality and quantity assurance methods; the audit process was introduced in January 1979. Adhering to accepted trends in hospital social work practice and to recommendations of authorities in the profession, members of the Department felt the impact of the implied meaning of accountability, measurement, case units, caseloads, productivity, documentation, effectiveness, and efficiency. In turn, these concepts precipitated departmental examination of resources which included staffing patterns, time, and space.

## Social Work Audits

Members of the Department completed two audits of social work technology. Accomplished in the Fall 1979, the first audit focused upon the "Social Work Assessment." Prepared in the Spring 1980, the second audit concern was with the "Social Work Plan." Now in preparation, the third audit centered objectives upon social work time utilization and patient-family needs.

In March 1980, through the Office of Clinical and Management Systems (OCAMS), the Social Work Department obtained a "baseline tape" of 622 computer-assisted social case records. According to OCAMS, the Department was the first to request baseline data. The 622 social work records were sorted from approximately 1,800 medical discharges from December 1, 1979 through February 29, 1980, with some "spill over" at either end of the time period. The baseline data may be used as a universe for future audits and other quality and quantity assurance methods.

## Interdepartmental Activities

Established April 18, 1979, the Nursing/Social Work Liaison Committee became an important linkage between the two disciplines for seeking solutions to

systems problems. After identifying the adolescent patient population as a special patient group requiring a continuum of services across Institute and Department lines, in May 1980, the Committee took the initiative to organize a Clinical Center-wide Committee on Adolescence. Served by representatives of Social Work, Nursing, Medicine, Clinical Pathology, Education and Patient Activities, this Committee entered planning stages for a symposium on the needs of adolescent patients and their multidiscipline caregivers. The Committee has aimed for wide attendance from members of the NIH-CC community.

Social workers were appointed to serve on Committees which included NINCDS Protocol Review Board, NHLBI Protocol Review Board, NEI Protocol Review Committee, NICHD Protocol Review Committee, NICHD Policy Committee, NIH-EEO-Federal Women's Program, Equal Opportunity Employment Committee, Awards Board-CC, and The NIH Recreation and Welfare Committee.

## III. MAJOR PROGRESS IN RESEARCH, SERVICES, TRAINING, AND DEVELOPMENT

### Research

Social workers participated in the following studies: the NCI Dermatology Service Study on Cystic Acne, the Pain Study of the NCI Medicine Branch, the Collaborative Study between NIAID/NIMH on the Psychodynamics of Hereditary Angioedema Patients, and the NIAMDD Study of Pregnancy and Lupus. In the Spring 1980, the Program Director, Division of Cancer Control and Rehabilitation, NCI, proposed a collaborative study of the Impact of Cancer on the Family.

As participants in these studies, social workers contributed content to the planning stages, prepared and administered questionnaires, and conducted pre-interim-post treatment interviews for psychosocial assessment.

### Training

From academic year 1970, the Social Work Department affiliated with local Schools of Social Work for the training of graduate level social workers.

During the early 1970s, the National Catholic School of Social Services, Catholic University of America, and the undergraduate Department of Social Work, George Mason University, placed students for field instruction. The School of Social Work and Community Planning, Maryland University at Baltimore, continued affiliation with the Department dating from September 1975. In August 1978, Howard University School of Social Work placed their first two students in field instruction with the Department.

From field placements during this reporting period, two Howard University students received their Masters Degree in May 1980. Two Maryland University students entered field placement in January 1980, and three students completed their field assignments in December 1979.

## Staff Education

The Department's standing Education and Training Committee, reorganized in November 1979, prepared to assess staff education and training from several viewpoints which included sharing the budget, training for supportive services inherent in staff and program development, promoting education for career interests and specialties, and utilizing NIH-Clinical Center resource persons and programs. Post-training/education accountability reports to the Department and program/service input to patients were considerations given high priority by the Committee.

A 15-hour Field Instruction-Consultation seminar was provided the Social Work Field Instructors. Scheduled over a 5-month period from January 1980, content of the seminar included review of field instruction techniques and course work expectations. A faculty member at the National Catholic School of Social Services, Catholic University of America, led the seminars.

Social workers enrolled in continued education programs which were sponsored by professional associations, psychiatric treatment settings, schools of social work, local universities, and speciality schools. Subject matter for these programs included family therapy, group psychotherapy, health issues, community resources, divorce, quality and quantity assurance, changes in hospital social work practices, adolescence, social work student teaching, and family systems.

## Community Related Activities

Members of the Department continued professional affiliations and patient service linkages with such organizations as the American Cancer Society, the Montgomery County Chapter of the American Red Cross, the Amyotrophic Lateral Sclerosis Society of America, the Muscular Dystrophy Association, the Division of Vocational Rehabilitation, the American Heart Association, the Area Chapter Mended Hearts, the Association of Pediatric Oncology Social Workers, the Association for Child Care in Hospitals, the Arthritis Foundation, the Volunteers for Visually Handicapped, and the Parkinsonian Society of Greater Washington, D.C.

## Patient Services

Increases in patient admission/discharge rates impacted upon delivery of social work services. Demands for discharge planning accelerated. The two Social Work Sections reported on searches for skilled nursing care facilities, terminal care facilities, homemaker services, foster homes, respite care services, and sheltered workshops. Material and facility complications included nursing home waiting lists, shortcomings in insurance programs, restrictions in Medicaid/Medicare programs, and searches for home care equipment.

Social workers intervened with crisis intervention methods and objectives, with extended and intensive casework, and with social group work. Alleviation and amelioration goals required multiple-level problem-solving approaches which ranged from Patient Emergency Fund allowances through one-to-one

counseling for medical-social adjustments and adaptations. Crisis intervention came into prominent use for the brief stay patients. These individuals required an almost immediate social work interview to assess coping strengths, to elicit needs for practical assistance, and to obtain appropriate community resources.

The social work group method served both inpatients and outpatients. Providing wider use of social work manpower, the method was used for social case finding, for orienting new patients/families to the biomedical research setting, for strengthening and reinforcing coping skills and for dealing with physical damage alterations to self-concept. NCI/NICHD Social Work Section reported nine active groups which served Special Ambulatory Care patients, clinic patients, inpatients, young adults, parents, and other family members; namely, Obesity Protocol Patient's Rap Session, Medicine Branch Screen Group, Breast Cancer Group, Surgery Branch Clinic Orientation Group, Heart/Cancer Protocol Support Group, Teen Group, Special Ambulatory Care Patients (SACP), Parent Group 2-East, and Parent Group 9-W. NHLBI Social Work Section established a Self-Help Cardiac Patient Orientation Group. The Lupus Rap Sessions, Arthritis Rap Sessions, and Rheumatoid Arthritis Patient Group were ongoing NIAMDD Social Work Section groups. NEI-Macular Degeneration Protocol Patient Group was organized in March 1980. The NINCDS Social Work Section established a Seizure Group in March 1980. Structurally, these groups were open-ended or closed, member-limited or time-limited, and informational or ameliorative.

Underlying the delivery of direct social services to patients was active social work contact with hospital and agency collaterals. In order to bring continuity and consistency to medical-social services, this important aspect of service delivery required collaborative and coordinated planning by all members of treatment units. Often discharge planning with agency collaterals either secured or prepared delivery of entitlements and resources for health and social maintenance of patients and families. Even so, psychosocial, socioeconomic, and regional disadvantages impinged upon the quality of discharge plans. Return to rural communities and small cities, where distances separated patients from social-health maintenance agencies, required resourceful adaptations of home care plans. Urban-based agencies presented entitlement eligibility constraints as well as higher costs for nursing care and respite services. These complications sometimes compromised short and long-range plans for post-hospital care.

International and nation-wide patient populations required the services of social workers for facilitating arrangements for transportation, lodging, and interpretors with much of the coordinating done prior to patient admission. Although a social-financial assessment by telephone left much to be desired, for the social worker it afforded an opportunity to establish a preadmission rapport with patients; for the patient, the early contact tended to reduce travel and arrival anxieties.

## Wig Contract

Approximately 235 wig requisitions were processed through the Social Work Department. Consistent with past utilization of this service, wig

requisitions were let in the amount of $23,065.00 during the nine months (October 1979 through June 1980) of FY 1980.

## Interment Allotments

Effective May 1977, the Department was assigned the decision-making responsibility for letting interment allotments. The following chart shows utilization frequencies over a 3-year period.

### UTILIZATION FREQUENCIES - INTERMENT ALLOTMENTS

| Fiscal Year | First Quarter | Second Quarter | Third Quarter | Fourth Quarter | Total |
|---|---|---|---|---|---|
| 1978 | 12 | 12 | 9 | 7 | 40 |
| 1979 | 16 | 7 | 7 | 17 | 47 |
| 1980 | 15 | 9 | | | 24 |

## On-Call System

Formalized in May 1977, the Department's On-Call System was designed to provide social work coverage through week-day evenings, week-ends, and holidays. The following chart is a 3-year, quarterly breakdown on the utilization of this service.

### UTILIZATION OF ON-CALL SYSTEM BY HOURS EFFECTIVE MAY 1, 1977

| Fiscal Year | First Quarter | Second Quarter | Third Quarter | Fourth Quarter | TOTAL |
|---|---|---|---|---|---|
| 1978 | 13hrs-33min | 25hrs-13min | 04hrs-15min | 11hrs-41min | 54hrs-42min |
| 1979 | 06hrs-15min | 08hrs-40min | 05hrs-05min | 10hrs-10min | 30hrs-10min |
| 1980 | 18hrs20min | 03hrs-41min | 03hrs-03min | - | 25hrs-03min |

## NIH Patient Emergency Fund

Administered through the Social Work Sections and Department, the Patient Emergency Fund provided an array of services to Clinical Center patients and families. Expenditures were for basic and miscellaneous necessities, local transportation for patients, room and board allowances for relatives, and special recreational programs for patient attendance. Well supported by members of the NIH Clinical Center community, the Fund has been kept viable by regular contributions, ingenious benefits, and memorial gifts. The utilization of Patient Emergency Funds is shown in the following chart.

## PATIENT EMERGENCY FUND BREAKDOWN

| | Deposits | Withdrawn | Average Exp. | Number of Patients Helped with PEF NCI | OTHER |
|---|---|---|---|---|---|
| July 1975-June 1976 | $37,000 | $47,900 | $172 | 169 | 109 |
| July 1976-June 1977 | $49,000 | $45,500 | $150 | 154 | 152 |
| July 1977-June 1978 | $53,00 | $62,300 | $216 | 145 | 144 |
| July 1978-June 1979 | $45,000 | $57,000 | $194 | 145 | 149 |
| July 1979-June 1980 | $27,400 | $62,400 | $193 | 167 | 157 |

## IV. FUTURE OBJECTIVES

1. Reaffirmation of the missions and goals of the Social Work Department with continuing emphasis on enhancing the excellence of medical care, maximizing the social functioning of individuals and families, and supporting and participating in the clinical research mission, i.e., (A) reviewing and updating departmental policies and procedures; and (B) developing a proposal for social work participation in research activity.

2. Establish a multi-purpose information system which utilizes the resources of the Office of Clinical and Management Systems (OCAMS).

   Purposes include:

   A. Establishment of managerial and clinical accountability systems.

   B. Provision of guideline data for social service program development.

   C. Provision of information for staff development in support of social service programs.

   D. Provision of retrievable source material for social work research in either a departmental or collaborative approach.

   E. Establishment of a unit of productivity which will provide a uniform workload measure to assure efficiency.

3. Expansion of the social work group methods that have been developed and a testing of their effects.

TABLE 1

FOUR-YEAR SUMMARY OF PATIENTS SERVED

| Patient Status | Patients Served July 1976 - May 1977 | | Patients Served July 1977 - May 1978 | | Patients Served July 1978 - May 1979 | | Patients Served July 1979 - May 1980 | |
|---|---|---|---|---|---|---|---|---|
| | Number | % of Total | Number | % of Total | Number | % of Total | Number | % of Total |
| Preadmission | 109 | 1.4 | 91 | 1.0 | 186 | 2.3 | 456 | 5.3 |
| Clinic | 587 | 7.5 | 1,014 | 12.0 | 640 | 7.8 | 757 | 8.7 |
| Follow-Up | 1,593 | 20.4 | 1,422 | 17.0 | 1,668 | 20.2 | 1,382 | 15.9 |
| Outpatients Total | 2,289 | 29.3 | 2,527 | 30.0 | 2,494 | 30.3 | 2,595 | 29.9 |
| Inpatients Total | 5,513 | 70.7 | 5,941 | 70.0 | 5,742 | 69.7 | 6,094 | 70.1 |
| GRAND TOTAL | 7,802 | 100.0 | 8,468 | 100.0 | 8,236 | 100.0 | 8,689 | 100.0 |

## TABLE 2
## INPATIENT COVERAGE BY PERCENTAGE

July 1979 through May 1980

| INST. | INPATIENT CENSUS | INPATIENTS SERVED | PERCENTAGE COVERAGE |
|---|---|---|---|
| NCI | 3,429 | 2,143 | 62.4 |
| NHLBI | 1,925 | 1,633 | 84.8 |
| NIAID | 1,005 | 679 | 67.5 |
| NIAMDD | 1,022 | 717 | 70.1 |
| NINCDS<br>NEI | 1,154 | 712 | 61.6 |
| NICHD | 589 | 468 | 79.4 |
| TOTAL | 9,124 | 6,352 | 69.6 |

July 1978 through May 1979

| INST. | INPATIENT CENSUS | INPATIENTS SERVED | PERCENTAGE COVERAGE |
|---|---|---|---|
| NCI | 3,506 | 1,899 | 54.2 |
| NHLBI | 1,934 | 1,352 | 69.9 |
| NIAID | 873 | 695 | 79.6 |
| NIAMDD | 967 | 692 | 71.6 |
| NINCDS<br>NEI | 1,037 | 693 | 66.8 |
| NICHD | 477 | 411 | 86.2 |
| TOTAL | 8,794 | 5,742 | 65.3 |

## TABLE 3
## Number of Clients Provided with Social Work Services
## July 1979 - June 1980

| | PREADMISSION | | INPATIENT | | CLINIC | | FOLLOW-UP | | TOTAL PTS. | TOTAL FAMILY MEMBS. |
|---|---|---|---|---|---|---|---|---|---|---|
| | Pt. | Family Memb. | Pt. | Family Memb. | Pt. | Family Memb. | Pt. | Family Memb. | | |
| 1979 JULY | 37 | | 581 | | 64 | | 130 | | 812 | |
| | | 13 | | 446 | | 36 | | 52 | | 547 |
| AUG. | 27 | | 602 | | 53 | | 153 | | 835 | |
| | | 9 | | 447 | | 40 | | 47 | | 543 |
| SEP. | 26 | | 552 | | 59 | | 173 | | 810 | |
| | | 19 | | 399 | | 39 | | 50 | | 507 |
| OCT. | 48 | | 576 | | 78 | | 103 | | 805 | |
| | | 16 | | 483 | | 46 | | 48 | | 593 |
| NOV. | 65 | | 582 | | 79 | | 99 | | 825 | |
| | | 38 | | 474 | | 32 | | 41 | | 585 |
| DEC. | 36 | | 472 | | 42 | | 90 | | 640 | |
| | | 26 | | 272 | | 31 | | 30 | | 359 |
| 1980 JAN. | 43 | | 523 | | 79 | | 113 | | 758 | |
| | | 29 | | 372 | | 51 | | 50 | | 502 |
| FEB. | 35 | | 535 | | 99 | | 101 | | 770 | |
| | | 15 | | 366 | | 37 | | 48 | | 466 |
| MAR. | 38 | | 548 | | 40 | | 161 | | 787 | |
| | | 23 | | 353 | | 32 | | 75 | | 483 |
| APR. | 46 | | 563 | | 90 | | 137 | | 836 | |
| | | 32 | | 352 | | 47 | | 73 | | 504 |
| MAY | 55 | | 560 | | 74 | | 122 | | 811 | |
| | | 35 | | 504 | | 26 | | 42 | | 607 |
| JUNE | 32 | | 556 | | 86 | | 109 | | 783 | |
| | | 29 | | 365 | | 41 | | 50 | | 485 |
| TOTAL | 488 | | 6,650 | | 843 | | 1,491 | | 9,472 | |
| | | 284 | | 4,833 | | 458 | | 606 | | 6,181 |

## TABLE 4

## Group Activity Report

Oct. 1979 - June 1980

| Section | Research Activities | | Practice-Prog. Activities | | Social Work Dept. Activities | | Com. and Prof. Activities | | Total Hours |
|---|---|---|---|---|---|---|---|---|---|
| | Hours | % | Hours | % | Hours | % | Hours | % | |
| NCI | 106 | 3.8 | 1,330 | 47.4 | 1,045 | 37.3 | 324 | 11.5 | 2,805 |
| NHLBI | 732 | 49.2 | 612 | 41.1 | 142 | 9.6 | 2 | 0.1 | 1,488 |
| NIAID | 369 | 66.2 | 158 | 28.3 | 31 | 5.5 | - | - | 558 |
| NIAMDD | 321 | 63.2 | 149 | 29.3 | 35 | 6.9 | 3 | 0.6 | 508 |
| NICHD | 367 | 71.8 | 144 | 28.2 | - | - | - | - | 511 |
| NINCDS/E | 346 | 50.8 | 233 | 34.2 | 78 | 11.5 | 24 | 3.5 | 681 |
| TOTAL | 2,241 | 34.2 | 2,626 | 40.1 | 1,331 | 20.3 | 353 | 5.4 | 6,551 |

## TABLE 5
## NIH PATIENT EMERGENCY FUND EXPENDITURES

*October 1979 - June 1980

| MONTH 1979 | SPECIAL PROGRAM | PATIENT TRANSPORTATION | ALLOWANCE TO RELATIVES | PATIENT MISCELLANEOUS | BASIC NECESSITIES | TOTAL WITHDRAWN | TOTAL DEPOSITS |
|---|---|---|---|---|---|---|---|
| OCT. | 996.00 | 579.25 | 5,869.26 | 415.50 | 211.00 | 8,071.01 | |
| NOV. | 781.50 | 390.30 | 5,708.00 | 756.92 | 183.00 | 7,819.72 | 2,412.50 |
| DEC. | 829.75 | 79.40 | 5,669.50 | 333.00 | 210.00 | 7,121.65 | 2,065.50 |
| 1980 JAN. | 856.50 | 292.00 | 5,746.50 | 384.89 | 200.00 | 7,479.89 | 3,676.00 |
| FEB. | 779.00 | 129.70 | 5,174.61 | 170.10 | 175.00 | 6,428.41 | 3,136.30 |
| MAR. | 804.00 | 313.00 | 4,012.50 | 260.45 | 201.00 | 5,590.95 | 3,215.45 |
| APRIL | 853.00 | 388.80 | 4,648.22 | 235.75 | 178.50 | 6,304.27 | 4,129.62 |
| MAY | 753.28 | 310.00 | 5,384.00 | 241.00 | 157.50 | 6,845.78 | 1,386.60 |
| JUNE | 1,168.00 | 234.00 | 4,856.50 | 245.76 | 182.50 | 6,686.76 | 7,347.55 |
| TOTAL | 7,821.03 | 2,716.45 | 47,069.09 | 3,043.37 | 1,698.50 | 62,348.44 | 27,369.52 |

*Nine months of FY 1980

October 1979 through September 30, 1980

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

# SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES CLINICAL CENTER

## DEPARTMENT OF SPIRITUAL MINISTRY

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October 1, 1979 through September 30, 1980

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
CLINICAL CENTER

## DEPARTMENT OF SPIRITUAL MINISTRY

### OVERVIEW

The basic task of the Department was to provide spiritual ministry to individual patients and their families who welcomed the ministrations of a clergyman and to hold religious services in the hospital. It also included acting as liaison with religious groups not represented by the staff chaplains. Fundamental to this task was the bedside ministry to patients and family members and the religious services held in the fourteenth floor Chapel. Other tasks of the Department included consulting with fellow staff members of the Clinical Center, attending multidisciplinary conferences, membership on research committees, working with the NIH EEO Council and EEO counseling, participating in education and orientation seminars, lecturing, and consulting with other clergy and community groups.

Statistics indicated the following average religious preferences of newly admitted patients: Jewish - 6%; Catholic - 27%; Protestant and others - 67%.

### STAFF

Chaplain LeRoy Kerney served as Chief of the Department and as a Protestant Chaplain. Chaplain Robert White and Chaplain William Payne were the other Protestant Chaplains. Chaplain Clinton Newton served as a part-time Protestant Chaplain from October to July.

Father Eugene Linehan, S.J. served in the hospital on a five day basis. Several part-time priests or pastoral associates assisted him in ministering to the patients and their families. They worked on days not covered by Father Linehan, brought Holy Communion to the bedside, made pastoral visits, and worked with many of the Spanish speaking families. A small group of seminarians from the School of Theology, Catholic University, came for supervised training during the school year.

Rabbi Joseph Levine served in the hospital on a half-time basis: Tuesdays, Thursdays, and Friday afternoons. He also served in a similar capacity

at St. Elizabeths Hospital, Washington, DC. He was available for emergencies at the Clinical Center through the paging system.

## CHAPEL SCHEDULE

Regular Chapel services were held during the year for the major faith groups. Mrs. Frances Viernstein was the Sunday Chapel organist. These services were:

Protestant: Sunday, 10:00 a.m. Holy Communion Service, the first Sunday of each month.

Catholic: Sunday and weekdays, 11:15 a.m. Daily distribution of Communion to bedridden patients.

Jewish: Friday, 4:30 p.m.

In addition to the regular services, these special services were held:

Protestant:
- World Wide Communion - 1st Sunday in October
- Thanksgiving Day
- Christmas Carol Service
- Christmas Day - bedside visitation
- Maundy Thursday
- Good Friday Service - (Participation by Protestant and Catholic Clergy and patients)

Catholic:
- Holy Days of Obligation Mass
- Special Blessing of Throats
- Distribution of Ashes - Ash Wednesday

Jewish:
- Rosh Hashana
- Yom Kippur
- Memorial Services
- Sukkot
- Chanukah
- Purim
- Passover
- Shavuoth

All three faiths extended the ministry of the Chapel services by broadcasting the services through bedside speakers for those unable to go to the Chapel and by visitation to bedridden patients. Appropriate sacraments were administered as requested.

## CHAPEL SERVICES

The Department attempted, when possible, to have a staff member visit all patients prior to major surgery, patients who were on the seriously ill list, and families of the patients who died. All Catholic patients were contacted through the sacramental ministry of the Catholic chaplain. The Jewish chaplain was able to see all the patients of the Jewish faith. Most of the Protestant patients were visited. Priority was given to visiting the terminally ill, the seriously ill, patients scheduled for surgery, referrals by staff, relatives and pastors, as well as direct patients' requests. Clergymen from the community were called upon to minister to special patients, e.g., patients requesting special rites from clergymen of their own denomination.

These included several Greek Orthodox priests who were routinely called to minister to the Greek-speaking patients.

Pastoral problems which the chaplains encountered included: loss of spiritual meaning, fear of death and the process of dying, lonliness, grief, fear, guilt, anxiety, boredom, identity crisis, changes in body-image and body-function. Pastoral methods included pastoral conversations, pastoral counseling, sacraments, blessings, prayer, scripture, and worship. On occasion, the chaplains helped patients and their families resolve dilemmas of conscience, conflicts of values, and difficulties in accepting radical therapies.

All members of the staff endeavored to be sensitive to the patient's own understanding of religion for himself, and, in turn, became a resource person for the patient to discover or rediscover his own spiritual strength. The complex work of a chaplain called for familiarity with the medical situation, medical knowledge, sensitivity to emotional issues, and work with staff and family.

Pastoral Ministry Statistics For Two Typical Months:

| | | Protestant | Catholic | Jewish |
|---|---|---|---|---|
| Admissions | October 1979 | 436 (71%) | 145 (24%) | 33 (05%) |
| | May 1980 | 413 (70%) | 150 (25%) | 32 (05%) |
| Discharges | October 1979 | 427 (72%) | 136 (23%) | 31 (5%) |
| | May 1980 | 449 (68%) | 174 (27%) | 32 (5%) |
| Pre-ops | October 1979 | 77 (64%) | 38 (31%) | 05 (05%) |
| | May 1980 | 80 (63%) | 28 (22%) | 18 (14%) |

## WORK WITH STAFF

Group seminars with staff members dealt with family, emotional, and treatment problems. Staff attended a number of weekly multidisciplinary meetings. Frequent informal consultation with nurses, doctors, and social workers concerning a particular patient's progress and condition was helpful in carrying out an effective plan of pastoral care and visitation.

## RESEARCH COMMITTEES

Chaplain Kerney was a member of the National Institute of Mental Health Research Review Committee on Behavioral Studies and of the National Institute of Neurological and Communicative Disorders and Stroke Research Review Committee.

## EEO

Chaplain White functioned as an EEO Counselor and as a member of the CC-EEO Advisory Committee and the NIH-EEO Advisory Council.

Chaplain White attended a week long evaluation and goal setting workshop for the NIH-EEO Advisory Council in Harpers Ferry, West Virginia.

## EDUCATION AND TRAINING

Chaplain Kerney was a panelist in a workshop on "Death and Dying" for Clinical Center staff personnel.

Chaplain Kerney served on an agenda committee for the Clinical Center for Issues of Patient Care in Biomedical Research.

Chaplain Payne was a member of a panel that dealt with the emotional needs of cancer patients for student nurses in the Cancer Institute.

## CONSULTATION

Rabbi Levine was invited to serve as a consultant to the Department of Pastoral Care at the Children's Hospital National Medical Center, Washington, DC.

## COMMUNITY EDUCATION

Chaplain White led a seminar on the "Clinical and Psychological Aspects of Death" for the Department of Sociology, Montgomery College.

Chaplain White led a Pastoral Care Workshop at the Warner Memorial Presbyterian Church, Kensington, Maryland.

Chaplain White spoke on "Pastoral Care to the Cancer Patient" at the Medical Breakfast, Bradley Hills Presbyterian Church, Bethesda, Maryland.

Chaplain White served as a Moderator at the Maryland Regional Meeting of the White House Conference on the Family.

Chaplain White led a workshop on "Religious Problems in Jewish-Christian Marriages"for the Jewish Social Service of Washington, DC.

Chaplain White continued as a panelist on the Bauman Television Programs on "The Presence of God" and an Easter Special.

Chaplain Payne shared in three memorial services during the year. His memorial remarks at one of the services was printed in the Congressional Record.

Father Linehan shared in a panel discussion with a Rabbi, Minister and Buddhist Monk at the Hospice Seminar in Northern Virginia, "Haven of Northern Virginia".

Father Linehan led a seminar at the Colonial Nursing Home for its medical staff on the needs of the terminally ill.

Rabbi Levine served on a panel devoted to mental health at the Annual Clergyday at the Veterans Administration Hospital, Washington, DC.

Rabbi Levine lectured to the Jewish Community of Leisure World about his work as a chaplain at the Clinical Center.

Rabbi Levine served on a special committee on Hospital Chaplaincy of the Washington Board of Rabbis.

## PROFESSIONAL MEETINGS AND TRAINING

Chaplain Kerney attended the annual meeting of the College of Chaplains, a Divison of the American Protestant Hospital Association, St. Louis, Missouri.

Chaplain White attended the Psychiatric Institute Foundation 2nd Annual Conference on Adolescent Psychotherapy.

Chaplain White attended the Psychiatric Institute Foundation Short Course on Adolescent Psychiatry.

Chaplain White took the NIH-CPR Course on the NIH campus.

Father Linehan attended the Sixth Training Institute on Theological Concerns of the Health Apostolate held by the Catholic Health Association in America, Philadelphia, Pennsylvania. He also received training in Prayer and Ministry by the Jesuits of the Maryland Province for a week in Pennsylvania.

Rabbi Levine conducted a workshop on "Clergy-Health Team Communication" at the annual meeting of the Association of Mental Health Clergy held in connection with the American Psychiatric Association, San Francisco, California.

Rabbi Levine led a workshop on "Pastoral Care" at the convention of the Central Conference of American Rabbis, Pittsburgh, Pennsyvania.

## PUBLICATIONS

Rabbi Levine had an article on pastoral care which was presented at a conference for Rabbis reprinted in the Military Chaplain's Review, Winter 1980.

Rabbi Levine wrote an article based on a week's activities as a Rabbi at the Clinical Center and St. Elizabeths Hospital which was printed in the Washington Post.

October 1, 1979, through September 30, 1980

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

# SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
# CLINICAL CENTER

## SURGICAL SERVICES DEPARTMENT

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October 1, 1979, through September 30, 1980

PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

# SUMMARY ANNUAL REPORT OF PROGRAM ACTIVITIES
# CLINICAL CENTER

## SURGICAL SERVICES DEPARTMENT

The Surgical Services Department was established as a new Clinical Center department in June, 1979.

### I. Mission and Goals

The Department has a threefold mission: to coordinate the activities required by the surgical components of the Institutes for the efficient management and operation of their programs; to provide the necessary personnel, space, equipment, and supplies for the program operation; to provide nonprofessional manpower, supplies and equipment for the Anesthesia contractor.

In order to achieve the above mission, the following goals have been identified and are being pursued.

A. Establish and maintain an environment that supports high morale and a committed, caring performance by all members of the staff.

B. Increase awareness of the role that aseptic technique plays in maintaining a safe environment for patients, personnel, and visitors.

C. Ensure accountable, ethical nursing practice.

D. Provide educational programs which update and augment the staff's knowledge.

E. Have each staff member develop individual goals.

F. Develop an ongoing cross-training of staff to meet elective and emergent patient care requirements in each of the surgical specialties.

G. Provide opportunities for the staff to develop better interpersonal relationships.

### II. Department Activities

A. The addition and training of six new staff nurses and one heart-lung machine technician alleviated the staff shortage encountered during the summer and fall of 1979.

B. Considerable amounts of time and planning were utilized in developing criteria for improvements to 10A Surgical Annex air handling equipment and physical plant.

C. In conjunction with the Clinical Center's newly created Materiel Handling Department and the Surgery Branch, NCI, specifications were drawn and procurement actions were initiated for all the fixed equipment required for the new surgical suite in the ACRF building.

D. Two staff nurses in the Department were among the first in the country to be certified for professional achievement by the Association of Operating Room Nurses.

III. Major Progress in Research, Services, Training, and Development

A. The Surgical Services Department continues to support the existing research protocols of the Institutes' surgical branches, as well as implementing new ones such as the Intra-operative Radiation Protocol for NCI's surgical branch.

B. Services have been provided for observational experiences in the surgical suites from within the Clinical Center, as well as for visitors from the outside.

C. The Department participated in the educational program for the Cancer Work Study students.

D. Over half of the surgical nursing staff have completed the basic CPR course.

E. Two head nurses have completed the Instructor's Training in CPR.

F. All the departmental staff received in-service training on Infection Control and Line Isolation and Ground Systems in the OR.

G. Other training provided for the staff included: Primary Nursing for Clinical Nurses; Implications of Anesthesia with IHSS Patients; Hepatitis B: A Hazard to Clinical Center Employees; Nursing Responsibility and the Patient's Right to Know; Nerve Injury from Positioning; Management of Heparin during Surgical Intervention.

H. Supervisory personnel attended a seminar on Motivational Dynamics.

I. Four staff members attended the Congress of the Association of Operating Room Nurses.

IV. Future Objectives

A. To increase cross-training of personnel until all staff are able to function in all surgical specialties.

B. Implementation of the new Clinical Center Dress Code protocol.

C. Complete the selection of equipment for the new ACRF surgical suite and prepare the staff for a smooth transition.

D. Redefine the responsibilities of the different sections in the Department in order to achieve a more efficient operation during our second year of existence.

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